In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: November 29, 2023

BRIAN ANKLAM and KAREN ANKLAM, as the legal representatives of the estate of their daughter, N.A., deceased,	*	PUBLISHED
Petitioners,	*	No. 17-2061V
v.	*	Special Master Nora Beth Dorsey
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Dismissal; Measles, Mumps, Rubella, Varicella ("MMRV") Vaccine; Seizure; Death.
Respondent.	*	

Curtis R. Webb, Monmouth, OR, for Petitioners.
Katherine Carr Esposito, U.S. Department of Justice, Washington, DC, for Respondent.

DECISION[1]

I. INTRODUCTION

On December 29, 2017, Brian Anklam and Karen Anklam ("Petitioners"), as legal representatives of the estate of their daughter, N.A., deceased, filed a petition for compensation under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42

[1] Because this Decision contains a reasoned explanation for the action in this case, the undersigned is required to post it on the United States Court of Federal Claims' website and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the Decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), Petitioners have 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access.

U.S.C. § 300aa-10 et seq. (2018).[2] Petitioners alleged that as a result of a Measles, Mumps, Rubella, Varicella ("MMRV") vaccine N.A. received on June 23, 2016, N.A. developed a fever, which triggered a seizure that caused her death.[3] Petition at 2-3 (ECF No. 1). Respondent argued against compensation, stating that "this case is not appropriate for compensation under the terms of the [Vaccine] Act." Respondent's Report ("Resp. Rept.") at 2 (ECF No. 9).

After carefully analyzing and weighing the evidence presented in this case in accordance with the applicable legal standards, the undersigned finds that Petitioners have failed to provide preponderant evidence that N.A.'s MMRV vaccine caused her death. Thus, Petitioners have failed to satisfy their burden of proof under Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1280 (Fed. Cir. 2005). Accordingly, the petition must be dismissed.

II. ISSUES TO BE DECIDED

There are two factual disputes. Joint Prehearing Submission, filed June 3, 2022, at 4 (ECF No. 72). The parties dispute whether N.A. suffered a seizure during the night of June 30, 2016 or the morning of July 1, 2016. Id. The parties also dispute whether N.A.'s autopsy slides show abnormalities in the hippocampus,[4] specifically granule cell dispersion and/or bilamination of the dentate gyrus.[5] Id.

Regarding causation, the parties agree the Court should apply Althen but disagree as to whether Petitioners have provided preponderant evidence of the Althen prongs. Joint Prehearing Submission at 4-5. The parties agree the MMRV vaccine can cause febrile seizures and that

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[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to -34 (2018) ("Vaccine Act" or "the Act"). All citations in this Decision to individual sections of the Vaccine Act are to 42 U.S.C.A. § 300aa.

[3] N.A. also received Haemophilus influenzae type B ("Hib"), pneumococcal conjugate ("Prevnar"), and Hepatitis A vaccines on June 23, 2016; however, Petitioners allege only the MMRV vaccine caused N.A.'s death. Petition at 2-3; Joint Prehearing Submission, filed June 3, 2022, at 4 (ECF No. 72).

[4] The hippocampus is "a convoluted elevation of gray matter extending the entire length of the floor of the temporal horn of the lateral ventricle; it is part of the limbic system and plays major roles in short-term memory and spatial navigation." Hippocampus, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=22696 (last visited Nov. 13, 2023). Hippocampus is used "to denote the entire structure, including the hippocampus proper (Ammon's horn), the dentate gyrus, and the subicular complex (presubiculum, parasubiculum, and subiculum), but it can also be used more restrictively, most often denoting the hippocampus proper, in which case the entire structure may be called the hippocampal formation." Id.

[5] Although not mentioned in the Joint Prehearing Submission, Petitioners' expert, Dr. Miller, also opined that there was an abnormality in the medulla. See Petitioners' Exhibit ("Pet. Ex.") 22 at 5, 8; Pet. Ex. 65 at 3; Transcript ("Tr.") 23, 46-49.

most of these seizures occur between seven to 10 days after MMRV vaccination. Id. at 4. However, they disagree as to (1) whether the MMRV vaccination administered to N.A. on June 23, 2016 caused her to have a vaccine-related seizure that led to her death, (2) whether an unobserved febrile seizure can cause a child to die, and (3) whether an unobserved febrile seizure did cause N.A. to die. Id.

III. BACKGROUND

A. Procedural History

Petitioners filed a petition along with medical records on December 29, 2017. Petition; Petitioners' Exhibits ("Pet. Exs.") 1-8. Petitioners filed medical literature on March 29, 2018. Pet. Exs. 9-12. Respondent filed his Rule 4(c) Report on May 25, 2018, arguing against compensation. Resp. Rept. at 2.

Petitioners filed an expert report from Dr. Marcel Kinsbourne on November 13, 2018 and an expert report from Dr. Douglas C. Miller on January 14, 2019. Pet. Exs. 13, 22. On May 30, 2019, Respondent filed expert reports from Dr. Christine McCusker, Dr. Sara O. Vargas, and Dr. Hart G.W. Lidov. Resp. Exs. A, C, E. Petitioners filed supplemental expert reports from Dr. Kinsbourne and Dr. Miller and photomicrographs of autopsy slides on November 4, 2019. Pet. Exs. 61, 65-66. From February to June 2020, Respondent filed supplemental expert reports from Dr. McCusker, Dr. Lidov, and Dr. Vargas. Resp. Exs. H-J.

The undersigned held a Rule 5 conference on August 18, 2020. Rule 5 Order dated Aug. 19, 2020 (ECF No. 53). Prior to the conference, the parties filed briefs. Resp. Pre-Rule 5 Conference Brief, filed Aug. 7, 2020 (ECF No. 51); Pet. Memorandum in Support of Rule 5 Ruling Favoring the Petitioners, filed Aug. 7, 2020 (ECF No. 52). The undersigned preliminarily found Petitioners' theory under Althen prong one may not be sound and reliable. Rule 5 Order at 1-2. The undersigned also preliminarily found no evidence that N.A. more likely than not suffered a seizure, and thus, given the lack of factual evidence and competing expert opinions, the undersigned was unable to conclude by preponderant evidence that N.A.'s hippocampus was pathologically abnormal. Id. at 2. As for the third Althen prong, the undersigned preliminarily found there was a temporal association but stressed that a temporal association alone is insufficient to prove causation. Id. Petitioners indicated their preference for an entitlement hearing, and one was set for January 2022. Id. at 2; Pre-Hearing Order dated Sept. 18, 2020 (ECF No. 55).

On September 20, 2021, Respondent filed additional medical literature. Resp. Exs. K-L. On November 24, 2021, Petitioners filed their pre-hearing submissions along with an expert report and medical literature from Dr. Miller and a case review report from Sudden Unexplained Death in Childhood ("SUDC") Registry and Research Collaborative ("SUDCRRC"). Pet. Prehearing Brief, filed Nov. 24, 2021 (ECF No. 58); Pet. Exs. 69-77. The undersigned held a status conference on December 9, 2021, on Respondent's request, due to Petitioners' recently filed expert report. Order dated Dec. 10, 2021 (ECF No. 64). Because Respondent's experts were unable to prepare responsive expert reports prior to the hearing, and because Petitioners

preferred to receive these reports prior to the hearing, the entitlement hearing was moved to July 2022. Id. at 1-2; Order dated Dec. 16, 2021 (ECF No. 66).

Respondent filed supplemental expert reports from Dr. Lidov and Dr. Vargas on February 28, 2022. Resp. Exs. M-N. Petitioners filed the parties' joint submission on June 3, 2022, and Respondent filed his pre-hearing submission on June 7, 2022. Joint Prehearing Submission; Resp. Pre-Hearing Submission, filed June 7, 2022 (ECF No. 73).

An entitlement hearing was held on July 12 and 13, 2022. Order dated July 14, 2022 (ECF No. 75); Transcript ("Tr.") 1, 219. Karen Anklam (N.A.'s mother), Dr. Miller, Dr. Kinsbourne, Dr. Lidov, Dr. Vargas, and Dr. McCusker testified. Tr. 3. Thereafter, additional medical literature and medical records were filed by the parties. Resp. Exs. U-Y; Pet. Exs. 78-80. In December 2022, Petitioners filed a post-hearing brief along with an affidavit from Mrs. Anklam, N.A.'s mother. Pet. Post-Hearing Brief, filed Dec. 13, 2022 (ECF No. 88); Pet. Ex. 81. On February 8, 2023, Respondent filed his post-hearing brief. Resp. Post-Hearing Brief, filed Feb. 8, 2023 (ECF No. 90). Petitioners filed a reply on March 13, 2023, and Respondent filed a sur-reply on April 4, 2023. Pet. Reply Brief, filed Mar. 13, 2023 (ECF No. 93); Resp. Sur-Reply, filed Apr. 4, 2023 (ECF No. 95).

This matter is now ripe for adjudication.

B. Factual History

1. Stipulated Facts

The parties agreed to the following stipulated facts as set forth in their Joint Prehearing Submission. See Joint Prehearing Submission at 1-4.

N.A. was born on June 18, 2015 in Saginaw, Michigan. Pet. Ex. 2 at 3. She was noted to be doing well with appropriate growth and development at her one-year well-child visit on June 23, 2016. Pet. Ex. 4 at 33. N.A. received Haemophilus influenzae type B ("Hib"), pneumococcal conjugate ("Prevnar"), Hepatitis A, and MMRV vaccinations on June 23, 2016 at the office of her pediatrician in Croswell, Michigan. Pet. Ex. 4 at 34.

N.A.'s parents took N.A. and her three siblings to a splash park for about two hours during the afternoon of June 30, 2016. Pet. Ex. 1 at 2; Pet. Ex. 5 at 5. N.A.'s mother thought that N.A. had developed a fever at about 6:00 p.m. on the evening of June 30, 2016. Pet. Ex. 1 at 3; Pet. Ex. 5 at 5. N.A.'s mother gave N.A. a 3.75 ml dose of Motrin and a tepid bath at about 6:00 p.m. Pet. Ex. 1 at 3; Pet. Ex. 5 at 5. N.A.'s mother put N.A. in her crib for the night at between 6:30 p.m. and 7:00 p.m. on June 30, 2016. Pet. Ex. 1 at 3; Pet. Ex. 5 at 5.

N.A. was found dead, face down in her crib, by her father, at about 9:00 a.m. on July 1, 2016. Pet. Ex. 1 at 3; Pet. Ex. 5 at 2, 5; Pet. Ex. 6 at 1. He reported that he first saw N.A.'s feet sticking out of the crib slats. Pet. Ex. 1 at 3; Pet. Ex. 5 at 3. He said that N.A.'s feet were purple, her arms were straight out at her elbows at her sides (like a star), and her face was

straight down to the mattress. Pet. Ex. 1 at 3; Pet. Ex. 5 at 3-5. He did not see anything coming out of N.A.'s mouth. Pet. Ex. 1 at 3.

N.A.'s father is an experienced paramedic. He immediately knew that N.A. was dead and had died some time before. Pet. Ex. 1 at 3; Pet. Ex. 5 at 5.

An autopsy of N.A. was done on July 3, 2016. Dr. Kanu Virani, M.D., the Forensic Pathologist who performed the autopsy, opined

> [N.A.] died of asphyxia. She was found dead face down in a crib. The entire autopsy failed to identify any natural disease. Children at age of one year and older should be able to turn side way or face up at the time of possible breathing difficulties during sleep. The entire autopsy and investigation surrounding her death[] failed to identify [a] possible factor for asphyxia. There are no physical injuries. The manner of death is undeterminable.

Pet. Ex. 6 at 1.

Other potentially relevant notations in the autopsy report include Dr. Virani's observations of a "[s]mall amount of mucus [] present in nostrils," that the "[t]he respiratory mucosa [was] mildly congested," a "[s]mall amount of mucus [] present in the trachea and bronchi," and that "[t]here [was] no laryngeal edema or upper airway obstruction." Pet. Ex. 6 at 2-3. Microscopic examination of the lungs showed congested septa and minimal chronic inflammation of the submucosa of the epiglottis. Id. at 4.

N.A.'s twin sister, L.A., slept in a separate crib in the same room as her sister. She also received an MMRV vaccination on June 23, 2016. During the evening of July 1, 2016, Mrs. Anklam noted that L.A. had a rash on her back and felt a little warm. She had an elevated temperature, less than 100°F. Pet. Ex. 1 at 4. Petitioners brought L.A. to the emergency room ("ER") at the local hospital on July 1, 2016. She had a temperature of 100.2°F (rectal) at the hospital. Pet. Ex. 1 at 4; Pet. Ex. 7 at 3.

N.A.'s older brother, L.B.A. (DOB: 04/25/2012), experienced febrile seizures on March 16, 2015, and August 28, 2016, and was seen in the hospital on July 17, 2016, for fever, vomiting, and being "somewhat dazed and not acting quite right." Pet. Ex. 1 at 4; Pet. Ex. 7 at 4-6, 9-14, 24-27.

2. Summary of Medical Records

In addition to the facts stipulated to by the parties, the following summary of facts provides additional relevant information.

N.A. was born on June 18, 2015, along with her twin sister, L.A., without complications. Pet. Ex. 2 at 3. N.A. had a heart murmur that was resolved by discharge on June 21, 2015. Pet. Ex. 3 at 6-8; Pet. Ex. 4 at 2. At discharge, N.A. had a normal examination and appeared healthy. Pet. Ex. 3 at 6-8.

N.A. visited her pediatrician, Dr. Matthew Gormley, regularly for well-child visits from June 2015 to March 2016. Pet. Ex. 4 at 2-17, 20-27. N.A. was noted to be doing well and had appropriate growth and development. Id. at 3, 7, 12, 15-16, 21-22, 26. At visits in September 2015 and November 2015, N.A. received Pediatrix (diphtheria-tetanus-acellular pertussis ("DTaP"), hepatitis B, and Polio), Hib, Rotarix (Rotavirus), and Prevnar vaccinations. Id. at 12, 16. N.A. received the third doses of Pediatrix and Prevnar at a visit in December 2015. Id. at 22. No adverse reactions were noted following these vaccinations. See id. at 12, 16, 22.

On November 23, 2015, N.A. presented to Dr. Gormley with "nasal congestion and cough/wheezing for the last [three] weeks." Pet. Ex. 4 at 18. She had no fever or chills. Id. Assessment was an upper respiratory infection. Id. Dr. Gormley noted it was likely a viral illness and recommended follow-up if no improvement. Id.

N.A. presented to Dr. Gormley's office on May 13, 2016. Pet. Ex. 4 at 28. N.A. had some congestion, slight swelling near the right eye, and some eye drainage the day prior. Id. By that morning, the right eye was red and swollen shut. Id. No fever was noted. Id. Assessment was cellulitis. Id. N.A. was prescribed Cephalexin and was directed to return in one week. Id.

On May 18, 2015, N.A. returned for a follow-up examination. Pet. Ex. 4 at 30. N.A.'s father reported her "eye [was] no longer red or swollen and [there was] no further drainage." Id. N.A. was tolerating the antibiotics well. Id. Physical examination was normal. Id. N.A. was noted to have a body mass index in the "5th percentile to less than 85th percentile for age." Id. Notes indicated N.A.'s cellulitis was "resolved." Id. N.A.'s parents were instructed to continue giving her Cephalexin twice daily. Id.

N.A. presented to Dr. Gormley for her one-year well-child visit on June 23, 2016. Pet. Ex. 4 at 32. She was not currently on any medications. Id. N.A. did not have a fever, cough, or breathing issues. Id. Physical examination was normal. Id. at 33. Dr. Gormley noted N.A. was "[d]oing well" and had "appropriate growth and development." Id. At this visit, N.A. received her third Hib, fourth Prevnar, first hepatitis A, and first MMRV vaccinations. Id. at 34. No adverse reactions were noted. See id. at 32-35.

On the morning of July 1, 2016, shortly after 9:00 a.m., N.A. was found unresponsive in her crib. Pet. Ex. 5 at 3. N.A. "had obvious rigor mortis and was cold to the touch." Id. at 3. She "also had pooling on her skin that indicated that she had been deceased for some time." Id. Time of death was placed between 9:00 p.m. and 10:00 p.m. on June 30, 2016. Id. at 6.

3. Sheriff's Records

The Sheriff's records indicated Officer Robby Joe Wendling arrived on scene at approximately 9:35 a.m. on July 1, 2016. Pet. Ex. 5 at 3. He entered N.A.'s room and noted she was face up, "had obvious rigor mortis[,] and was cold to the touch." Id. She "also had pooling on her skin that indicated that she had been deceased for some time." Id.

Detective Mark Ruggles and Sergeant Shelly Park arrived on the scene shortly thereafter. Pet. Ex. 5 at 4. Detective Ruggles noted rigor mortis was fixed, livor mortis was consistent with Mr. Anklam's description that N.A. was found face down in a blanket, and N.A. was cold to the touch. Id. Detective Ruggles examined N.A. and found no injuries. Id.

The Incident Report documented that Petitioners took their children, including N.A., to the Splash Pond until 5:15 p.m. on June 30, 2016. Pet. Ex. 5 at 5. Once the family arrived home, the children were fed chicken noodle soup for dinner and then given a bath. Id. Mrs. Anklam stated N.A. was running a low-grade fever and given Motrin around 6:00 p.m. Id. Around 6:30 p.m., the children were put to bed. Id. Petitioners reported they did not hear anything from L.A. and N.A.'s room during the night. Id.

Mrs. Anklam stated she woke up around 6:30 a.m. and did not check on N.A. prior to leaving for work. Pet. Ex. 5 at 5. Mr. Anklam stated he went into L.A. and N.A.'s room around 9:00 a.m., when he found L.A. awake. Id. While changing L.A.'s diaper, he noticed N.A.'s "feet were just outside the rails of the crib." Id. He noticed "some discoloring to [N.A.'s] feet" and felt they were cold. Id. He turned her over and saw "she was 'pooling.'" Id. "[Mr. Anklam] stated that he knew right away that she was dead." Id.

Petitioners reported that N.A. "ha[d] been running a low grade fever, sometimes up to 100.5 since [June 19, 2016]." Pet. Ex. 5 at 5. The fever would fluctuate and sometimes dissipate. Id. Other than that, N.A.'s only other issue since birth was right eye swelling in May 2016. Id.

Time of death was placed between 9:00 p.m. and 10:00 p.m. on June 30, 2016. Pet. Ex. 5 at 6.

4. Autopsy[6]

An autopsy was conducted by Dr. Virani on July 3, 2016. Pet. Ex. 6 at 1. Autopsy findings indicated asphyxia with pulmonary edema and blanching on face. Id. Dr. Virani opined

> [N.A.] died of asphyxia. She was found dead face down in a crib. The entire autopsy failed to identify any natural disease. Children at age of one year and older should be able to turn side way or face up at the time of possible breathing difficulties during sleep. The entire autopsy and investigation surrounding her death[] failed to identify [a] possible factor for asphyxia. There are no physical injuries. The manner of death is undeterminable.

Id.

External examination noted "[b]lanching . . . in central portion of the face" and "[s]mall amount of mucus present in nostrils." Pet. Ex. 6 at 2. Internal examination revealed the "hippocampi [were] without abnormality." Id. There was no abnormality of the head or brain.

[6] For additional facts and findings found during the autopsy, see Pet. Ex. 6.

Id. "There [was] no laryngeal edema or upper airway obstruction." Id. at 3. Examination of the respiratory system revealed "[p]ulmonary edema and congestion," "[s]mall amount of mucus . . . in trachea and bronchi," and "mildly congested" respiratory mucosa. Id.

Microscopic examination of the lungs revealed "edema fluid and scatter macrophages[7] in alveoli,"[8] congested septa,[9] and "[m]inimal chronic inflammation . . . in the submucosa of epiglottis." Pet. Ex. 6 at 4. There was no acute or chronic inflammation in the trachea or bronchi and no evidence of aspirated foreign material and inflammation in airways or alveoli. Id.

Dr. Virani examined sections of the brain and did not find any abnormality. Pet. Ex. 6 at 4. He also reviewed "[s]ections of brain, heart, liver, spleen, thymus, kidneys, thyroid, adrenals, pituitary, stomach, intestines, appendix, pancreas, lymph nodes, bone marrow[,] and urinary bladder" and reported that they were all "unremarkable." Id. Additionally, toxicology testing did not reveal any positive findings. Id. at 5-6.

Dr. Virani documented the date of death to be "June 30, 2016, unknown PM." Pet. Ex. 6 at 1.

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[7] A macrophage is a "form[] of mononuclear phagocytes found in tissues" that "arise from hematopoietic stem cells in the bone marrow." Macrophage, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=29296 (last visited Nov. 13, 2023). Macrophages engage in "[p]hagocytic activity" and are also "involved in cell-mediated immune responses." Stedman's Medical Dictionary 1141 (28th ed. 2006). Phagocytosis is the process by which "particulate material, such as microorganisms or cell fragments[,] . . . is taken into the cell in membrane-bound vesicles (phagosomes) that originate as pinched-off invaginations of the plasma membrane. Phagosomes fuse with lysosomes, forming phagolysosomes in which the engulfed material is killed and digested." Phagocytosis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=38307 (last visited Nov. 13, 2023).

[8] An alveolar macrophage is "a rounded granular type, found within the alveoli of the lungs and serv[es] to ingest inhaled particulate matter." Alveolar Macrophage, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=87677 (last visited Nov. 13, 2023). Alveolus is "a small saclike structure" found in the lungs. Alveolus, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=2006 (last visited Nov. 13, 2023).

[9] Septum is "a dividing wall or partition." Septum, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=45434 (last visited Nov. 13, 2023). Septa can "separate adjacent pulmonary alveoli, containing connective tissue constituents of the respiratory tissue and the capillary network of the blood supply of the lung." Interalveolar Septum, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=105585 (last visited Nov. 13, 2023).

5. SUDC Registry and Research Collaborative Case Review Report

Petitioners participated in the SUDCRRC, consenting to have N.A.'s case reviewed. This collaborative "analyzes cases of sudden unexpected deaths in children to understand risk factors and causes and to develop preventative measures by studying available records . . . and performing genetic analyses and special studies." Pet. Ex. 77 at 3.

As part of the case review, N.A.'s parents were interviewed. In the interview on September 1, 2016, N.A.'s parents (Petitioners) reported no concerns about N.A.'s development. Pet. Ex. 77 at 5. During her life, N.A. had "no known seizures." Id. During the last 48 hours of her life, N.A. was "[c]ongested occasionally, but otherwise fine." Id. In her last 24 hours, N.A. "had a minor cold and [] appeared 'worn out, but not lethargic.'" Id. She also had a low-grade fever. Id. She was given one dose of Motrin after her dinner at 6:00 p.m. Id. at 5, 8.

Autopsy tissue of the brain (3 slides) was reviewed by the SUDCRRC neuropathologist who found no significant histopathology. Pet. Ex. 77 at 8. Further, "[t]he SUDCRRC Forensic Pathology reviewers were in complete agreement with the reviews of the study's . . . neuropathologist." Id. Based on their review, the "forensic pathologist consider[ed] the significant findings . . . to be: 1) [s]ibling with genetic syndrome associated with slightly prolonged QT,[10] 2) [s]ibling with febrile seizures, 3) [f]ound prone with face pressed into mattress with blanching lividity on face." Id. at 8-9. Under cause of death, the report concluded N.A.'s death was an "[u]nexplained sudden death," with intrinsic factors including "[f]ebrile at time of death and evidence of immune activation" and extrinsic factors including "[f]ound prone with face down with blanching." Id. at 9. The manner of death was "[u]ndetermined." Id. The report was signed by Dr. Orrin Devinsky, Principle Investigator. Id. at 10.

A SUDCRRC genetic panel was also performed for N.A. and "[n]o clinically significant variants [were] identified." Pet. Ex. 80 at 2.

6. Mrs. Anklam's Affidavit & Hearing Testimony

Mrs. Anklam is N.A.'s mother. Tr. 6; Pet. Ex. 1 at ¶ 1. She works as a nurse anesthetist, and her husband, Mr. Anklam, is a paramedic. Tr. 225; Pet. Ex. 1 at ¶¶ 19, 33.

N.A. was born on June 18, 2015. Pet. Ex. 1 at ¶ 2. She had a heart murmur that resolved prior to discharge. Id. "[N.A.] was healthy and developing normally until her sudden death on June 30, 2016." Id. at ¶ 3. Her "development was normal" and she was "always fed well." Id. at ¶¶ 4-5.

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[10] "A prolonged QT interval is an irregular heart rhythm that can be seen on an electrocardiogram. It reflects a disturbance in how the heart's bottom chambers (ventricles) send signals. In a prolonged QT interval, it takes longer than usual for the heart to recharge between beats." Prolonged QT Interval, Mayo Clinic, https://www.mayoclinic.org/diseases-conditions/long-qt-syndrome/multimedia/prolonged-q-t-interval/img-20007972 (last visited Nov. 13, 2023).

On June 23, 2016, N.A. received her third Hib, fourth Prevnar, first hepatitis A, and first MMRV vaccinations at the office of her pediatrician, Dr. Gromley. Pet. Ex. 1 at ¶ 6. Although she cried after receiving the vaccinations, her "behavior was pretty normal." Id. at ¶¶ 7-8. For the first two days following the vaccinations, Mrs. Anklam gave N.A. Motrin. Id. at ¶ 8. Because she was getting her first molars, "she was a little more cranky and drooling more than usual." Id. "[N.A's] behavior was unremarkable from June 23 to June 29." Id. at ¶ 9.

On the morning of June 30, 2016, N.A. was well. Tr. 6. That afternoon, around 3:00 p.m., Petitioners took their children, including N.A., to a splash park. Tr. 6-7; Pet. Ex. 1 at ¶ 10. "[N.A.] was a bit crankier than usual, but it was a warm day, and [Mrs. Anklam] attributed it to that." Pet. Ex. 1 at ¶ 10. They arrived home around 5:00 p.m. and had chicken noodle soup for dinner, which ended sometime between 5:30 p.m. and 5:45 p.m. Tr. 7, 14; Pet. Ex. 1 at ¶ 11. "N.A. was very sleepy." Tr. 8; see also Pet. Ex. 1 at ¶ 11.

Following dinner, both N.A. and her twin sister, L.A., felt warm. Tr. 8; Pet. Ex. 1 at ¶ 12. Because of her experience as a mother and a nurse, Mrs. Anklam did not take their temperatures. Tr. 8; Pet. Ex. 1 at ¶ 13. She bathed both N.A. and L.A. together and noted they were both fine at the time. Tr. 9. Following the bath, Mrs. Anklam gave both N.A. and L.A. Motrin around 6:30 p.m., before putting them to bed in the same room in separate cribs sometime between 7:00 p.m. and 7:30 p.m. Tr. 9-10, 14; Pet. Ex. 1 at ¶ 14.

During the night, Petitioners did not hear anything from N.A.'s room. Pet. Ex. 1 at ¶ 15. N.A. and L.A. had been sleeping longer, and Petitioners attributed it to a growth spurt. Id. at ¶ 16.

The following morning, July 1, 2016, Mrs. Anklam left home at 6:30 a.m. to go to work. Tr. 10. She did not check on N.A. and L.A. prior to leaving for work. Tr. 10-11. Mr. Anklam went into N.A. and L.A.'s room around 9:00 a.m. that morning. Pet. Ex. 1 at ¶ 17. "When he glanced at [N.A.'s] crib, he knew something was wrong. Her feet were sticking out of the crib slats and her arms were straight at the elbows and out to her sides (like a little star)." Id. at ¶ 18. He saw N.A.'s feet were purple, she was face down, and "[t]here was nothing coming out of her mouth." Id. at ¶ 19. "He picked [N.A.] up and knew she was dead and had been for a while." Id. at ¶ 20. He then called 911 and Mrs. Anklam. Id.

Mrs. Anklam testified that she never saw N.A. have a seizure or knew her to have a fever in excess of 100°F. Tr. 15.

Mrs. Anklam testified the none of the three other children were ill on June 30, 2016, or showed symptoms of infection on July 1, 2016. Tr. 12. However, during the evening of July 1, 2016, around 7:00 p.m., Petitioners took N.A.'s twin sister L.A. to the ER because she had a slightly elevated fever and a rash on her back. Tr. 11; Pet. Ex. 1 at ¶¶ 21, 24. Mrs. Anklam averred that she was terrified to put her to bed because Petitioners did not know what led to N.A.'s death. Pet. Ex. 1 at ¶¶ 21-22. A thorough work up was completed and L.A. was discharged shortly after 9:00 p.m. Id. at ¶ 24.

After N.A. passed, Petitioners enrolled their family in a study of SUDC. Pet. Ex. 1 at ¶ 26. "Throughout [their] participation in that study []and [Mrs. Anklam's] own efforts to understand [N.A.'s] death[], [she] [] learned medical literature links [SUDC] to unobserved febrile seizures," which she averred "seem[s] especially relevant to [N.A.'s] death because MMRV vaccinations cause fevers and febrile seizures in the second week after vaccinations." Id. at ¶¶ 27-28.

Additionally, Mrs. Anklam explained that one of her sons had suffered three febrile seizures, and "[she] learned that children who die unexpectedly often have a history of febrile seizures or a family history of febrile seizures." Pet. Ex. 1 at ¶¶ 28, 41. His first seizure occurred on March 16, 2015. Id. at ¶ 30; Tr. 14-15, 224. On that day, he complained of ear pain and he had a "high normal" temperature below 100°F. Tr. 224; Pet. Ex. 1 at ¶ 30. He was given Motrin. Tr. 224; Pet. Ex. 1 at ¶ 30. While at the park over one hour later, he began seizing. Tr. 224-25; Pet. Ex. 1 at ¶¶ 31-32. When they arrived at the ER, his temperature was between 103°F and 104°F. Tr. 225; Pet. Ex. 1 at ¶ 35. He had two subsequent febrile seizures in July and August 2016. Pet. Ex. 1 at ¶¶ 36-40. He had genetic testing done that showed he had a 3q26 microdeletion, which Mrs. Anklam testified is not associated with seizures. Tr. 16, 223. Additionally, following N.A.'s passing, the other three children received cardiac evaluations, and all three were cleared. Tr. 15.

C. Expert Reports

1. Petitioners' Expert, Dr. Douglas C. Miller, M.D., Ph.D.[11]

a. Background and Qualifications

Dr. Miller is an anatomic pathologist and a neuropathologist. Tr. 18. He received his B.A. in biology from Williams College in Massachusetts and his M.D. and Ph.D. in physiology and biophysics from the University of Miami in Florida. Pet. Ex. 23 at 1. Thereafter, he completed an anatomic pathology residency and a neuropathology residency at Massachusetts General Hospital. Id. Dr. Miller has held various teaching and consulting positions throughout his career. Id. at 3-4. He currently works as a Professor in the Department of Pathology and Anatomical Sciences at the University of Missouri Medical Center, is the Chair of the Department of Pathology, and is the Director of the Pathology Residency Program. Tr. 18-19. He has authored or co-authored almost 300 publications. Pet. Ex. 23 at 7-27. Dr. Miller has served as a neuropathology consultant for medical examiners for over 30 years and he has "extensive experience with the neuropathology of sudden infant death." Pet. Ex. 22 at 2-3.

[11] Dr. Miller testified at the hearing and submitted three expert reports. Tr. 3; Pet. Exs. 22, 65, 69. Some of Petitioners' medical literature contains pagination that begins at page one, and others begin at varying page numbers. To avoid confusion, the undersigned used pagination consistent with the ECF pagination for the medical literature that did not begin at page one.

b. Opinion[12]

Dr. Miller opined that the MMRV vaccination administered to N.A. on June 23, 2016 led to a fever on June 30, that provoked a seizure that night, which caused N.A.'s death. Tr. 21-22, 25, 34-35.

i. Background

Dr. Miller discussed the relevant syndromes, including sudden unexplained death in children ("SUDC"), sudden infant death syndrome ("SIDS"), and sudden unexplained death in epilepsy ("SUDEP"), and briefly explained their relevance to this case. He classified N.A.'s case as SUDC, or sudden unexplained death in a young child over the age of one year when "there is no identified underlying disease or cause of death, including after a thorough autopsy, to which death can be attributed, plus a detailed scene investigation which confirms that the environment . . . cannot be blamed for [the child's] death." Pet. Ex. 22 at 5; see also Tr. 42.

He did not classify N.A.'s case as SIDS given her age at death[13] because SIDS "is defined as the sudden unexpected death of a child older than [one] month of age and no older than one year of age, for which no anatomic or toxicological cause of death can be found after a thorough scene investigation and thorough complete autopsy." Pet. Ex. 22 at 5; see also Tr. 41-42. Dr. Miller noted, however, "such arbitrary limits" between SUDC and SIDS "have little scientific basis." Pet. Ex. 22 at 5. Although N.A.'s autopsy did not conclude that she had SUDC or SIDS, he found these terms have bearing on N.A.'s cause of death because their risk factors, including sleeping position and fever,[14] are relevant to this case. Id. at 4; Tr. 42-43.

Lastly, Dr. Miller did not classify N.A.'s case as SUDEP because she did not have epilepsy, which by definition, requires two unprovoked seizures separated in time. Tr. 45, 67.

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[12] At the hearing, Dr. Miller testified that his opinions in his first expert report regarding "vaccine adjuvants and cytokines . . . [are] not relevant to this case." Tr. 61; see Pet. Ex. 22 at 9-12. He also retracted his opinions related to "the hypercarbia theory where there was a build-up of carbon dioxide." Tr. 61; see Pet. Ex. 22 at 6-12. As such, the undersigned will not address these opinions.

[13] At the hearing, and in his expert reports, Dr. Miller argued that N.A. was born slightly early at 36 weeks and 3 days, and thus, her actual age at death could be calculated to be less than one year, which would make this a SIDS case. Pet. Ex. 22 at 5; Tr. 41-42. The undersigned does not find this opinion affects her opinions or is determinative, and therefore, she will not address it.

[14] Dr. Miller acknowledged that vaccination is not a risk factor but noted that fever is a risk factor, and fevers are associated with vaccinations, including MMRV. Tr. 43. Dr. Miller was an expert in the Boatmon case, where the Federal Circuit held that mere evidence that it was "medically plausible" that the premature infant's death was caused by vaccinations failed to demonstrate a causal connection required for compensation under the Vaccine Act. Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351 (Fed. Cir. 2019). In this case, Dr. Miller testified that he did not "plan on relitigating Boatmon . . . . That's not what this case is about." Tr. 43.

Dr. Miller agreed that there was no evidence that N.A. ever had another seizure, which he opined is common in SUDC cases. Tr. 43.

ii. Althen Prong One

Dr. Miller opined the MMRV vaccine can lead to fever and febrile seizure, and a seizure can lead to death. Pet. Ex. 22 at 8. As an overview, Dr. Miller opined that a child who receives an MMRV vaccine has "a significant risk of fever and febrile seizures," and "[s]uch seizures, occurring unwitnessed in sleep, would present a significant risk of death in a child with a dysplastic dentate gyrus (the hippocampal abnormality associated with SUDC), with or without defects in the medullary 5HT system (such as the abnormality in the accurate nuclei associated with SIDS)." Id. He further opined that the risk of death is greater in a child with both defects. Id. He opined that "[t]his chain of events represents a highly plausible, scientifically valid, hypothesis." Id. at 13.

He explained that the MMRV vaccine can lead to fevers and seizures seven to 10 days after vaccination. Pet. Ex. 22 at 8, 12; see Tr. 34, 39; Pet. Ex. 19 at 2;[15] Pet. Ex. 21 at 2, 4-5.[16] "Fever is one of the consequences of the vaccination," explained Dr. Miller, "and fever can predispose to seizures." Tr. 34. He testified that "[a]ll people . . . have some risk . . . of having a febrile reaction to a vaccine." Id. For the MMRV vaccine in particular, Dr. Miller noted there is a "significantly greater risk of febrile seizures with a peak period of around seven to 10 days after the vaccination." Id. He acknowledged that such an event is "rare" but maintained that there is a "significantly increased risk" of fever and febrile seizures following the MMRV vaccine. Tr. 23-24, 58, 60.

Dr. Miller then explained that febrile seizures "certainly can lead to death in a vulnerable patient." Tr. 37. "Seizures represent an electrical storm . . . that affects the brain and leads to a number of other things that can happen." Id. For example, "electrical impulses from the cerebral hemispheres where the seizures occur[] can be transmitted down into the brainstem and the brainstem controls both respiratory effort and heart rate." Id. Thus, "a sudden electrical discharge can shut down the medulla and cause cessation of breathing and/or cardiac arrhythmia." Id. This "electrical activity may also stimulate an outpouring of autonomic nervous system activity," which can lead to "a discharge of sympathetic [] neurons [that] can also lead to cardiac arrhythmia and death." Tr. 37-38.

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[15] Nicola P. Klein et al., Safety of Measles-Containing Vaccines in 1-Year-Old Children, 135 Pediatrics e321 (2015).

[16] Shannon E. MacDonald et al., Risk of Febrile Seizures After First Dose of Measles-Mumps-Rubella-Varicella Vaccine: A Population-Based Cohort Study, 186 Canadian Med. Ass'n J. 824 (2014).

Next, he discussed the significance of abnormalities in the hippocampal and medullary brain tissue in sudden and unexpected deaths of children.[17] Pet. Ex. 22 at 5-9. He stated that the literature shows "a significant association between finding [] dentate gyrus abnormalities in children who have died in sleep and found dead, usually in a prone position, and with no anatomic cause of the death." Tr. 24-25. Literature has also "made an explicit connection [] suggest[ing] these children died in sleep or emerging from sleep at a time when the brain is more vulnerable to epileptogenesis, especially when the dentate gyrus, which normally acts as a sort of electrical gate to tamp down neuronal activity in the hippocampus, is defective." Pet. Ex. 65 at 2. Additionally, children with "hippocampal abnormalities at autopsy either themselves had a previous febrile seizure or had a first- or second-degree relative who had a febrile seizure history," and thus, Dr. Miller opined there is "an increased risk for this kind of sudden unexplained death when there's a family history of febrile seizures." Tr. 26, 33.

He testified that the hippocampus is located in the temporal lobe, with one on each side or hemisphere of the brain. Tr. 22. "[I]t is a very important structure in formation and consolidation of memories, other kinds of structures which are generally referred to as part of the limbic system, . . . and is frequently associated with temporal lobe seizures." Tr. 22-23; see, e.g., Pet. Ex. 28 at 9, 11.[18]

Dr. Miller opined that a "finding frequently found in autopsies of children whose death is classified as SUDC, SIDS[,] and [SUDEP]" is "dentate gyrus dysplasia, with what is termed granule cell dispersion including bilamination." Pet. Ex. 22 at 4-5 (internal quotations omitted)

[17] At the hearing, Dr. Miller also maintained febrile seizures can be fatal, even without hippocampal abnormalities. Tr. 51, 54.

[18] Marco M. Hefti et al., Hippocampal Malformation Associated with Sudden Death in Early Childhood: A Neuropathologic Study, 12 Forensic Sci. Med. & Pathology 14 (2016).

(citing Pet. Ex. 18;[19] Pet. Ex. 25;[20] Pet. Ex. 26;[21] Pet. Ex. 27;[22] Pet. Ex. 28; Pet. Ex. 29)[23] (noting this abnormality on autopsy "is believed to be related to an increased risk of seizures and sudden death related to seizures"); see also Tr. 69. The dentate gyrus is thought to govern nerve impulses in the hippocampus, and when it is dysplastic or abnormal, seizures may be generated. Pet. Ex. 69 at 2. Granule cell dispersion is an "abnormality of the gyrus in which some cells are located beyond the normal boundaries of that narrow line." Pet. Ex. 65 at 1. Bilamination, a form of dispersion, "describes lines of such granular cells outside the normal boundaries of the gyrus parallel to the direction of the gyrus."[24] Id. at 2.

Also, according to Dr. Miller, a brain abnormality in the medullas of infants is seen in over 70% of SIDS cases. Pet. Ex. 22 at 5, 8; Pet. Ex. 65 at 3. These abnormalities "involv[e] one or more parts of a network of neurons utilizing serotonin (5HT) as a neurotransmitter." Pet. Ex. 65 at 3 (citing, e.g., Pet. Ex. 67;[25] Pet. Ex. 68);[26] see also Pet. Ex. 22 at 5, 8. Dr. Miller explained that "[t]he neurons of this network have their developmental origins in cells from the embryonic rhombic lip, and so other abnormalities of rhombic-lip derived structures may suggest that there are abnormalities of the 5HT system, even though those specific abnormalities may not be detectable at autopsy except by special research techniques" not routinely availability in forensic autopsies. Pet. Ex. 65 at 3; see also Pet. Ex. 22 at 5, 8. "The inferior olivary nuclei are

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[19] Hannah C. Kinney et al., Sudden Death, Febrile Seizures, and Hippocampal and Temporal Lobe Maldevelopment in Toddlers: A New Entity, 12 Pediatric & Developmental Pathology 455 (2009).

[20] Michael L. Rodriguez et al., Hippocampal Asymmetry and Sudden Unexpected Death in Infancy: A Case Report, 8 Forensic Sci. Med. & Pathology 441 (2012).

[21] Hannah C. Kinney et al., Dentate Gyrus Abnormalities in Sudden Unexplained Death in Infants: Morphological Marker of Underlying Brain Vulnerability, 129 Acta Neuropathologica 65 (2015).

[22] Marco M. Hefti et al., Sudden Unexpected Death in Early Childhood: General Observations in a Series of 151 Cases, 12 Forensic Sci. Med. & Pathology 4 (2016).

[23] Hannah C. Kinney et al., Hippocampal Formation Maldevelopment and Sudden Unexpected Death Across the Pediatric Age Spectrum, 75 J. Neuropathology & Experimental Neurology 981 (2016).

[24] Citing an article from Dr. Kinney, Dr. Miller noted "the minimum number of cells to qualify for bilamination would be eight." Tr. 31; see also Pet. Ex. 65 at 2. It is not clear from the record which article Dr. Miller was referring to.

[25] Y. Ozawa & N. Okado, Alteration of Serotonergic Receptors in the Brain Stems of Hyman Patients with Respiratory Disorders, 33 Neuropediatrics 142 (2002).

[26] Y. Ozawa & S. Takashima, Developmental Neurotransmitter Pathology in the Brainstem of Sudden Infant Death Syndrome: A Review and Sleep Position, 130S Forensic Sci. Int'l S53 (2002).

also rhombic lip derivatives," and thus, "the presence of the gaps in neuronal populations . . . are evidence of such medullary abnormalities." Pet. Ex. 65 at 3.

Dr. Miller testified that the mechanism at play in a SUDC case "may be similar or identical" to the mechanism purported in SUDEP, described in more detail below. Tr. 67-68. He also explained that the literature has reported three main commonalities in SUDC cases: (1) "the deceased young child[] ha[s] a high frequency of a family history of febrile seizures;" (2) the child is "almost always found dead in bed, in a prone position;" and (3) the autopsy discloses hippocampal dysplasia. Pet. Ex. 22 at 5; see also Pet. Ex. 65 at 2; Pet. Ex. 74.[27] For support, Dr. Miller discussed various articles from Kinney et al. and others who described abnormalities in the hippocampus that they associated with sudden unexpected death, fever, and a family history of febrile seizures. Pet. Ex. 65 at 2.

In 2009, Kinney et al. examined 64 cases of sudden death in children aged one to 5.9 years to determine whether SUDC "is characterized by hippocampal and temporal lobe maldevelopment and an individual and/or family history of simple febrile seizures." Pet. Ex. 18 at 1. In the 49 SUDC cases, 28% had a familial history of febrile seizures, 98% were found during sleep, and 79% were found in the prone sleep position. Id. at 1, 10 tbl.1. Twenty-six of the 49 SUDC cases had hippocampal sections available for examination, and 16 of these cases (16/26 or 62%) had hippocampal abnormalities. Id. at 5, 10 tbl.1. When compared to non-SUDC cases, Kinney et al. found SUDC cases had more hippocampal abnormalities (62% versus 22%). Id. at 5.

Kinney et al. separated their data into three groups—SUDC with a personal history of febrile seizures, SUDC with a family history of febrile seizure, and SUDC with no personal or family history of seizures. Pet. Ex. 18 at 11 tbl.2. Seven SUDC cases had a family history of febrile seizures. Id. In this group, three children had hippocampal areas available for examination, and two of these three exhibited hippocampal abnormalities, specifically in the dentate gyrus. Id. at 5, 11 tbl.2, 12 tbl.3. Additionally, four of the seven (57%) had fever and all seven (100%) were found in their sleep in the prone position. Id. at 11 tbl.2.

Based on this study, Kinney et al. stated "that a subset of SUDC cases is characterized by an individual and/or family history of febrile seizures and hippocampal maldevelopment." Pet. Ex. 18 at 5. They hypothesized a new entity of SUDC cases "defined by unwitnessed sleep-related, sudden death and hippocampal/temporal lobe maldevelopment and characterized by an individual and/or family history of febrile seizures and prone sleep position, often face-down, at discovery." Id. They stressed the "defining feature[s]" of this entity are abnormalities in the hippocampus and temporal lobe and "individual and/or family histories of febrile seizures are important risk factors for sudden death in association with this [] pathology." Id. at 5-6.

Kinney et al. further stated that the abnormalities seen in the temporal lobe, in conjunction with SUDEP cases, "suggests the possibility that affected toddlers experience an unwitnessed, sleep-related seizure that originates in the anomalous epileptogenetic focus in the

[27] Jenna Harowitz et al., Seizure-Related Deaths in Children: The Expanding Spectrum, 62 Epilepsia 570 (2021).

hippocampus, resulting in upper airway occlusion/cardia arrythmia/hypotension, and fetal cardiopulmonary arrest." Pet. Ex. 18 at 6. They "speculate[d]" that in this entity of SUDC cases, "a terminal and fatal seizure leads to death . . . due to seizure-induced upper airway occlusion, augmented by airway compression in the prone (face-down) position." Id. Respiratory tract infections were noted as a "potential triggering factor." Id.

In 2014, Kinney et al. examined 153 autopsies of infants with sudden and unexpected death and found hippocampal pathology—bilamination and granule cell dispersion—present in 47 of 114 (41.2%) of the unexplained death group and 3 of the 39 (7.7%) of the explained death group. Pet. Ex. 26 at 2, 6. A 2016 article authored by Kinney et al. stated that hippocampal abnormalities in the dentate gyrus were associated with sudden death in children regardless of age. Pet. Ex. 29 at 3. Kinney et al. examined 32 cases with hippocampal abnormalities, 17 of which were over the age of one. Id. at 4. Of those 17 cases, 16 were sleep-related deaths and 13 were found in the prone position. Id. at 4 tbl.1. Dentate bilamination was found in 31 of the 32 cases, or 18 of the 19 children over one year of age. Id. at 5. Additionally, nine cases had a family history of seizures and 22 had a family history of febrile seizures and/or epilepsy. Id. Kinney et al. stated that "[t]he neuropathological findings . . . provide[d] a plausible mechanism for sudden and unexpected death via an epilepsy-like mechanism." Id. at 13. Specifically they stated seizures "may be generated in the abnormal [hippocampus]" and "triggered by stress (e.g. asphyxia or fever)." Id. None of the Kinney et al. articles discussed vaccinations, or any potential role of vaccinations.

Similar findings were reported by Hefti et al.[28] in 2016. Pet. Ex. 28. Hefti et al. examined 83 cases with at least one hippocampal section for microscopic review. Id. at 5. They classified these 83 cases into subgroups, including a subgroup of SUDC without hippocampal pathology or febrile seizure phenotype (22/83) and a subgroup termed "hippocampal maldevelopment associated with sudden death," or HMASD (40/83). Id. at 2. For the HMASD cases, 95% died during sleep and 85% were discovered in the prone position. Id. at 5. Twenty-five of the 40 (62.5%) had a personal and/or family history of febrile seizures, and 15 of the 40 (37.5%) had only a family history of febrile seizures. Id. Additionally, 20 had a fever within 48 hours of death. Id. at 6 tbl.2. For the 22 SUDC cases without hippocampal pathology or febrile seizure phenotype, 13 (59.1%) had a fever within 48 hours of death, 21 (95.5%) died during sleep, and 13 (61.9%) were found in the prone position. Id.

Hefti et al. hypothesized that the death in the HMASD cases "may be related to an unwitnessed seizure during sleep that originates in the malformed hippocampus," which they noted "is supported by the reported association of hippocampal malformations in [SUDEP] [and] those in HMASD." Pet. Ex. 28 at 9. They also hypothesized that "potential triggering events are sleep itself, fever, unwitnessed febrile seizure, and/or prone sleep." Id. Because none of the deaths in the HMSAD cases were witnessed, Hefti et al. concluded that "the direct relationship of febrile seizures (or hippocampal maldevelopment) to death is unknown." Id. at 11.

[28] Dr. Kinney is also an author on this publication.

Kon et al. (2020)[29] reviewed cases of SIDS (358), SUDC (48), and SUDEP (18) to determine the prevalence of hippocampal abnormalities, history of seizures, and demographic features. Pet. Ex. 73 at 2. Their findings revealed hippocampal abnormalities[30] associated with temporal lobe epilepsy in 16 of 36[31] (44.4%) of SUDC cases. Id. at 2, 5 tbl.2. Five of 11 SUDC cases with a history of afebrile seizures demonstrated hippocampal abnormalities, and none of the four SUDC cases with a history of febrile seizures displayed abnormalities in their hippocampus.[32] Id. at 2, 10. Most SUDC cases (27) were found in the prone position and half (24) experienced illness[33] within their last 72 hours. Id. at 5 tbl.2.

The authors noted that "[a]s hippocampal abnormalities are strongly associated with epilepsy, . . . researchers [have] hypothesize[d] that SUDC is 'epilepsy in situ.'" Pet. Ex. 73 at 10. Although none of their SUDC cases with a febrile seizure history had hippocampal abnormalities, the authors noted such link is well-documented and analogous to SUDEP, opining "[h]ippocampal abnormalities could predispose certain individuals to seizures in the event of a precipitating event such as infection." Id. Because hippocampal abnormalities were more likely to be seen in SUDC and SUDEP cases, the authors "suggest[ed] that the hippocampus likely plays a major role in SUDC and SUDEP." Id. at 11. Additionally, because an association between a history of seizures and prone sleeping position has been suggested, the authors noted a "possible explanation . . . is that these children may had experienced an unwitnessed seizure whilst in a prone position and being unable to free themselves from this position, asphyxiate, resulting in death." Id. at 10.

Dr. Miller acknowledged that a more recent article from 2021, authored by Leitner et al.,[34] reported "the lack of association of hippocampal findings in SUDC in controls as well as inconsistency of observations by multiple blinded reviewers indicates discrepancy with previous studies." Tr. 53-54 (citing Resp. Ex. K at 2); see also Pet. Ex. 69 at 3. In Leitner et al., hippocampal specimens from 19 SUDC and 26 sudden explained deaths in children ("SEDC") control cases were reviewed by nine different reviewers from three types of pathologists (forensic pathologists, neuropathologists, and dual-certified neuropathologists/forensic pathologists). Resp. Ex. K at 1, 3. The reviewers reported a similar frequency of findings

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[29] Fu Chuen Kon et al., Hippocampal Abnormalities and Seizures: A 16-Year Single Center Review of Sudden Unexpected Death in Childhood, Sudden Unexpected Death in Epilepsy and SIDS, 16 Forensic Sci. Med. & Pathology 423 (2020).

[30] For the specific hippocampal abnormalities seen, see Pet. Ex. 73 at 8 tbl.6.

[31] Only 36 of the 48 SUDC cases had this information available. Pet. Ex. 73 at 5 tbl.2, 7.

[32] Family history of seizures was not documented. See Pet. Ex. 73.

[33] Fever was not included in this category. Pet. Ex. 73 at 4 tbl.1.

[34] Dominique F. Leitner et al., Blinded Review of Hippocampal Neuropathology in Sudden Unexplained Death in Childhood Reveals Inconsistent Observations and Similarities to Explained Paediatric Deaths, 2021 Neuropathology & Applied Neurobiology 1.

relative to the hippocampal slides from the SUDC and control cases. Id. at 9. Also, the reviewers were in agreement about hippocampal findings in SUDC cases with or without a history of febrile seizure. Id. However, "half of the slides were reported as abnormal (SUDC 52.5%, control 53.0%), indicating a potential range in as yet unidentified normal variation, undiagnosed pathology[,] or phenomena unrelated to SUDC or febrile seizures." Id. The authors concluded that the "discordance among reviewer groups indicates a discrepancy with previous studies and a need for larger consensus studies to standardise hippocampal findings to identify both the range of normal variation and pathology or phenomenon unrelated to SUDC or febrile seizures." Id. at 11.

Dr. Miller argued the study "ha[d] multiple flaws," including a lack of critical analysis as to whether the cause of death was correctly determined by the original pathology, which "could have [] tainted" the control group with cases that should have been classified as SUDC and were not. Pet. Ex. 69 at 3.

Dr. Miller also discussed an unpublished study he worked on that found dentate gyrus dysplasia "is very common in the general autopsy population at all ages and with [various] causes of death." Pet. Ex. 22 at 6; see also Pet. Ex. 69 at 3-4. The study was a retrospective review of autopsies with neuropathology examinations from 2008 through 2016. Tr. 41; Pet. Ex. 69 at 3. In total, 962 autopsies were examined, including all age ranges. Tr. 41; Pet. Ex. 69 at 3. Dr. Miller explained that 201 of the 962 displayed "at least one dentate gyrus with dysplasia, whether granule cell dispersion with or without bilamination, duplications, or hyperconvolutions (or combinations thereof)." Pet. Ex. 69 at 3. He concluded that "in the general autopsy population, including cases of SIDS, SUDC, and SUDEP, there were dentate gyrus abnormalities in 20.8% of the cases." Id. The study population had 11 cases of SUDC, seven (63.6%) of which had definite dentate gyrus abnormalities. Id. at 4. Given this data, Dr. Miller asserted "the incidence of dentate gyrus dysplasia in SUDC cases . . . is at least [three] times that in the general population (63% to 21%)." Id. He acknowledged, however, that he did not have statistical testing completed on this data. Id. As of July 2022, his study was not yet peer-reviewed or sent for publication. Tr. 40. Nor was the study filed in this case.

Two case reports were filed by Petitioners. Dlouhy et al.,[35] in 2017, described a child with a history of two witnessed complex febrile seizures who died suddenly and unexpectedly following a suspected unwitnessed seizure during sleep; the death was classified as a SUDEP. Pet. Ex. 70 at 2. The authors wrote, "[a]lthough some cases of [SUDC] have a history of febrile seizures, no documented case of febrile seizure-induced death has been reported." Id. They suggested that "febrile seizures can lead to sudden unexpected death in children through mechanisms similar to those involved in SUDEP." Id. at 4. However, Dlouhy et al. acknowledged that a seizure may not have occurred. Id. The authors did not discuss vaccines.

[35] Brian J. Dlouhy et al., Unexpected Death of a Child with Complex Febrile Seizures—Pathophysiology Similar to Sudden Unexpected Death in Epilepsy?, 8 Frontiers Neurology 1 (2017).

Similarly, Myers et al. (2017)[36] reported the case of a 20-month-old girl with a complex chromosomal disorder and episode of febrile status epilepticus,[37] who died suddenly and unexpectedly during a video electroencephalogram ("EEG"). Pet. Ex. 71 at 2. The "sequence of physiologic changes leading up to death suggest[ed] a pathophysiology similar to [SUDEP]." Id. The child did not meet the criteria for an epilepsy diagnosis, and thus the death was classified as a SUDC. Id. at 4. However, the authors suggested that the mechanism of her death was "SUDEP-like" following febrile seizure. Id. at 5. Vaccinations were not at issue.

Dr. Miller acknowledged that epidemiological studies have conflicting findings regarding a connection with vaccination and sudden unexpected deaths. Pet. Ex. 22 at 9. He cited various studies that found no causal relationship between vaccinations[38] and sudden unexpected deaths. See, e.g., Pet. Ex. 40 at 2;[39] Pet. Ex. 41 at 3 (finding "no way to prove that the[ir] infant deaths [were] caused by vaccination");[40] Pet. Ex. 44 at 18 (concluding "[t]he evidence does not indicate a causal relation between [diphtheria-pertussis-tetanus ("DPT")] vaccine and SIDS").[41] He also cited studies on SIDS. See, e.g., Pet. Ex. 45;[42] Pet. Ex. 46 at 2 ("There is no increased or reduced risk of sudden infant death during the period after the vaccination.").[43] He argued that there are various flaws in these studies, and in his view, epidemiology "does not provide any answer to the question of a possible causal relationship between vaccinations and SIDS." Pet. Ex. 22 at 9. However, Dr. Miller maintained "there is a scientifically and medically plausible means to connect these events." Id.

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[36] Kenneth A. Myers et al., Sudden Death After Febrile Seizure Case Report: Cerebral Suppression Precedes Severe Bradycardia, 140 Pediatrics 1 (2017).

[37] Status epilepticus is "a prolonged series of seizures without return to full consciousness between them." Status Epilepticus, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=108327 (last visited Nov. 13, 2023).

[38] MMRV and MMR vaccinations were not included in these studies.

[39] Rüdiger von Kries et al., Sudden and Unexpected Deaths After the Administration of Hexavalent Vaccines (Diphtheria, Tetanus, Pertussis, Poliomyelitis, Hepatitis B, *Haemophilius Influenzae* Type B): Is There a Signal?, 164 Eur. J. Pediatrics 61 (2005).

[40] B. Zinka et al., Unexplained Cases of Sudden Infant Death Shortly After Hexavalent Vaccination, 24 Vaccine 5779 (2006).

[41] Inst. of Med., Evidence Concerning Pertussis Vaccines and Deaths Classified as Sudden Infant Death Syndrome, in Adverse Effects of Pertussis and Rubella Vaccines 125 (Christopher P. Howson et al. eds., 1991).

[42] M.M.T. Vennemann et al., Do Immunizations Reduce the Risk for SIDS? A Meta-Analysis, 25 Vaccine 4875 (2007).

[43] Ronny Kuhnert et al., Reanalyses of Case-Control Studies Examining the Temporal Association Between Sudden Infant Death Syndrome and Vaccination, 30 Vaccine 2349 (2012).

Dr. Miller concluded that his theory, or "chain of events[,] represents a highly plausible, scientifically valid, hypothesis." Pet. Ex. 22 at 13. He acknowledged "[t]here are no experimental or clinical studies possible to fully prove [his] hypothesis" in this case. Id.

iii. Althen Prongs Two and Three

Dr. Miller opined the MMRV vaccination administered to N.A. on June 23, 2016 caused N.A. to develop a fever, and this vaccine-induced fever provoked a seizure on June 30 that resulted in N.A.'s death due to her unknown vulnerability. Tr. 21-22, 25, 34-35; Pet. Ex. 69 at 1-2.

First, he noted there is evidence N.A. had a fever on the night of June 30, 2016, within the risk period following MMRV vaccines. Pet. Ex. 22 at 4, 12. He explained Petitioners reported on the morning of July 1, 2016 that N.A. "had been having episodic low grade fever, up to 100.5°F, since [June 13]," although "[t]his [was] not mentioned in the pediatrician's records for the [June 23] visit." Id.; see also Tr. 34.

Dr. Miller opined that the fact that N.A. received Motrin around 7:00 p.m. on June 30 does not suggest N.A. did not suffer a fever or febrile seizure. Tr. 234. He found this argument "speculative" and he argued that "Motrin is not 100[%] effective in reducing or preventing fever" and "Motrin won't affect the development of fever." Tr. 234-35. But see Pet. Ex. 21 at 7 ("If MMRV continues to be offered for first-dose administration, it might be advisable to counsel parents regarding antipyretic use if children experience a fever within the peak risk period.").[44]

Dr. Miller next opined N.A. suffered a seizure during the night of June 30, 2016 and cited four reasons for support: (1) N.A.'s family history of seizures; (2) N.A. received an MMRV vaccination within the appropriate time period; (3) N.A. was found dead in the prone position; and (4) N.A.'s autopsy abnormalities. Tr. 25-26.

First, he noted N.A. had a positive family history of seizures (her brother), which he opined was evidence in favor of a finding that N.A. suffered a seizure on the night of June 30, 2016. Tr. 25-26. Dr. Miller noted N.A.'s brother's 3q29 microdeletion syndrome is separate from his history of febrile seizures because seizures have not been found to be related to a 3q29 microdeletion syndrome. Tr. 231-32, 248; see also Pet. Ex. 79 at 8 (finding "seizures are not a significant part of the 3q29 deletion phenotype," and thus, "the neurodevelopmental pathway affected by 3q29 deletion is . . . not [relevant to] epilepsy or seizure").[45]

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[44] Dr. Miller agreed this happened here. Tr. 248-49. An antipyretic is "an agent that relieves fever." Antipyretic, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=3479 (last visited Nov. 13, 2023).

[45] Megan R. Glassford et al., Novel Features of 3q29 Deletion Syndrome: Results from the 3q29 Registry, 170 Am. J. Med. Genetics 999 (2016).

Second, he noted N.A. received an MMRV vaccination seven to 10 days prior to her development of a fever and her death, which is within the risk period for seizures post-MMRV vaccination. Tr. 25, 34. Third, N.A. was found dead in a prone position, which he explained "is a common position for those with SUDEP, . . . [SUDC], and [] in SIDS." Tr. 25.

And fourth, he opined N.A.'s autopsy supports a finding that N.A. suffered a seizure the night of June 30 because (1) no definite cause of death was found on autopsy and (2) N.A.'s brain slides showed abnormalities consistent with SUDC. Tr. 25-26. Specifically, the autopsy and police investigation showed no evidence of trauma, no toxins, no anatomical cause of death (no infectious process), no developmental abnormality, and "no specific finding" as to what caused N.A.'s death. Tr. 22, 25-26; Pet. Ex. 22 at 4. Additionally, Dr. Miller examined the autopsy slides and found most showed "no significant abnormality of any kind, no infectious process, no developmental abnormality, [and] no signs of trauma." Tr. 22. However, he observed two significant abnormalities on the brain slides that he explained were commonly seen in SUDC cases in association with febrile seizures. Tr. 25-26, 35; Pet. Ex. 22 at 12.

According to Dr. Miller, the first abnormality was in N.A.'s hippocampus, which he explained exhibited a dysplastic, or abnormally formed, dentate gyrus. Tr. 23, 28-29 (citing Pet. Ex. 66 at 3); see also Pet. Ex. 22 at 4-6. Specifically, he found granule cell dispersion including bilamination.[46] Tr. 23, 28-29 (citing Pet. Ex. 66 at 3, 7); see also Pet. Ex. 22 at 4-6.

The second brain abnormality Dr. Miller found on the autopsy slides dealt with the medulla. Tr. 23. He opined "the slide of the medulla showed some patches in the medulla which were lacking neurons[] [and] lacking nerve cells, suggestive of a developmental abnormality or perhaps other unappreciated episodes of anoxia in the medulla, although there were no other signs of anoxia anywhere else in the brain." Id. Specifically, he found a "subtle depletion of large neurons from each inferior olivary nucleus along with a mild gliosis" and he opined this finding has been reported in autopsies of SIDS cases. Pet. Ex. 22 at 5, 8; see also Tr. 46-49; Pet. Ex. 65 at 2-3; Pet. Ex. 66 at 9. This abnormality is "thought to indicate either a developmental abnormality in medullary structures derived from the embryonic rhombic lip, or prior unrecognized episodes [] from which there had been spontaneous recovery." Pet. Ex. 22 at 5, 8; see also Pet. Ex. 65 at 3. Dr. Miller opined that if N.A.'s case was viewed as a SIDS case, instead of SUDC, "the olivary abnormalities" would be "evidence of a rhombic lip problem that likely also affected some parts of the medullary 5HT system and predisposed [N.A.] to sudden death with exposure to additional risk factors," or fever. Pet. Ex. 65 at 3.

Because of the abnormalities identified by Dr. Miller in the brain autopsy slides, he opined N.A.'s MMRV vaccine put her at "greater risk." Tr. 25. He opined that "more likely than not[,] these abnormalities represent the underlying vulnerability that made [N.A.'s] death possible." Pet. Ex. 22 at 7. He found it "likely that both abnormalities played a role in [N.A.'s] death" because there are "connections between the medullary systems governing respiration and the cerebral hemispheric limbic system, notably the hippocampi." Id. During the hearing, Dr. Miller testified that the abnormality in N.A.'s hippocampus would be sufficient to have caused

[46] For a further discussion of Dr. Miller's opinions on bilamination, in general and in N.A.'s case, see Tr. 226-31, 235-37; Pet. Ex. 65 at 1-2; Pet. Ex. 26 at 8; Pet. Ex. 28 at 4.

her death. Tr. 50. He explained that "for those cases where there's been an autopsy with a neuropathology examination, there's a very strong indication that the hippocampal abnormalities are associated with a vastly increased risk, more than three times [the] risk, over the general population." Tr. 51-52; see also Pet. Ex. 69 at 4.

If, however, there were no abnormalities in the brain at autopsy, Dr. Miller concluded it would be "unknown" as to whether the vaccine was involved in N.A.'s death. Tr. 51 (stating "presumably" febrile seizures can be fatal in the absence of hippocampal abnormalities).

During the hearing, Dr. Miller was questioned about the report from SUDCRRC, specifically the fact that the neuropathologist and forensic pathologist who reviewed the brain slides did not report any abnormalities, which he did not review prior to or during the hearing. Tr. 237-38. He could not account for why he found abnormalities in the hippocampus when the SUDCRRC noted no abnormalities. Tr. 238-41. Dr. Miller testified that he was unable to comment without knowing the neuropathologist that examined the hippocampus or what slides of the hippocampus were examined. Id.

Next, Dr. Miller compared the facts in N.A.'s case to those deaths that occur in those with epilepsy. Tr. 35-36. He explained "[it is] very well documented that patients who have a known history of epilepsy have an increased risk for sudden unexpected death, those deaths almost always [] com[e] out of sleep or during sleep, [and they are] almost always found in bed face down." Tr. 36. Such cases are referred to as SUDEP, although he agreed that N.A.'s case was not SUDEP. Tr. 36, 42, 45.

On cross-examination, Dr. Miller maintained that the "terminal event" in N.A.'s case was a febrile seizure that led to apnea or cardiac arrhythmia and cardiac arrest. Tr. 62. He acknowledged that his theory is "not very well understood because it's such a rare event and [there have] been no animal model or human studies which have fully documented in a large enough number of cases to have some certainty about the actual mechanism." Id. He opined there was a "very small" likelihood that N.A. could suffer from apnea or cardia arrhythmia and cardiac arrest without the MMRV vaccination. Id. But he emphasized that "SUDC is a very rare event[,] . . . far less common than SIDS." Id.

Dr. Miller had no opinion on how long N.A.'s seizure lasted. Tr. 44-45. Given his experience in forensic pathology and as a medical examiner, he opined that the time of death is "highly subjective" and "subject to many variables." Tr. 246. Time of death is "an approximation" that "could be off by several hours in either direction." Id.

Regarding Dr. Vargas' opinion that N.A. had a viral infection at the time of death, Dr. Miller responded by opining that it was "implausible" without better evidence. Tr. 58-59. But see Pet. Ex. 22 at 8 (noting N.A. "did not clearly have an upper respiratory infection prior to her death, although the intermittent low grade fever . . . might represent such condition"). Dr. Miller was also not persuaded by Dr. Vargas' opinion that N.A. had a chronic respiratory viral infection. Pet. Ex. 65 at 3-4.

On July 1, 2016, N.A.'s sister, L.A., had "yellow nasal crusting." Tr. 59. Dr. Miller agreed this would indicate an infection, which he called a "common cold." Id. He opined that a cold is not usually associated with a fever. Tr. 59-60. Even if N.A.'s twin sister L.A. had a viral infection on July 1, Dr. Miller maintained that N.A.'s fever would still be caused by her MMRV based on "statistics." Tr. 60. His reliance on statistics is that "children get colds, and they don't generally die of them. . . . There is a described increased risk for both fever and febrile seizures in children who got the MMRV vaccine . . . . It's still a very rare event, but it's a definite increased incidence." Id.

Further, Dr. Miller was not persuaded by Dr. McCusker's arguments that N.A.'s mucus in her airways led to her death. Pet. Ex. 65 at 3. Dr. Miller argued Dr. McCusker misstated the autopsy findings because only a "[s]mall amount of mucus" was present. Id. (quoting Pet. Ex. 6 at 2). He asserted that Dr. McCusker's theory, which is based on the belief that infants only breathe out of their nose and cannot switch to breathing out of their mouth, is without foundation. Id.

He concluded that the combination of factors here, including N.A.'s fever on the night of June 30, 2016, N.A.'s receipt of MMRV vaccination seven days prior, N.A.'s family history of seizures, N.A.'s prone position on death, and N.A.'s autopsy findings, constitutes compelling evidence that N.A.'s MMRV vaccination triggered a fever that led to a seizure that subsequently caused her death. Tr. 34-36, 69; Pet. Ex. 69 at 2.

2. Petitioners' Expert, Marcel Kinsbourne, M.D.[47]

a. Background and Qualifications

Dr. Kinsbourne is a neurologist and pediatric neurologist. Tr. 88-89. In 1955, he obtained his B.M., B.Ch. from Oxford University Medical School, and he completed postdoctoral training through 1964 in the United Kingdom. Pet. Ex. 14 at 1. Thereafter, he obtained board certification and licensing in the United States and Canada and worked as a professor at various teaching institutions. Id. at 1-2. Dr. Kinsbourne has served and is currently serving on a number of editorial boards. Id. at 3-4. He has authored or co-authored more than 400 publications. Id. at 5-39. Dr. Kinsbourne is no longer a practicing physician and no longer works as a professor at the New School University in New York. Tr. 90. He has not practiced clinical medicine or worked in a hospital since 1981. Id.

b. Opinion

Dr. Kinsbourne opined that "more likely than not[,] [] the fever and seizure generated by the MMRV [vaccination] was . . . the cause of [N.A.'s] death." Tr. 78; see also Pet. Ex. 13 at 4; Pet. Ex. 61 at 3.

[47] Dr. Kinsbourne provided two expert reports and testified at the hearing. Pet. Exs. 13, 61; Tr. 3. Dr. Kinsbourne cited and discussed some of the same literature as Dr. Miller. For sake of brevity, the undersigned will not repeat those studies.

i. Althen Prong One

Dr. Kinsbourne opined that the MMRV vaccine can trigger an unwitnessed seizure that can cause death. Pet. Ex. 13 at 3-4; Pet. Ex. 61 at 2-3.

Dr. Kinsbourne began by explaining that is it well-known that the MMRV vaccine can cause fevers and febrile seizures between seven to 10 days post vaccination. Tr. 76; see also Pet. Ex. 19 at 2; Pet. Ex. 21 at 2; Pet. Ex. 61 at 1. He testified that "the MMRV vaccination is . . . the most prone to cause the adverse effects of fever and seizure, in other words, febrile seizure, within an appropriate time frame." Tr. 78-79. According to Dr. Kinsbourne, a child who receives an MMRV vaccination is seven times more likely to have a seizure seven to 10 days following administration. Tr. 79, 105. He also opined that a fever increases the risk of a seizure, especially in children between the ages of six months and six years, with a peak at year two. Tr. 80. At the hearing, Dr. Kinsbourne did not indicate which studies support these statistics. In his expert reports, he cited studies that compared the risk of seizures between the MMRV vaccine and the MMR and separate varicella ("MMR+V") vaccines. See Pet. Exs. 19, 21. MacDonald et al. showed that the risk of seizures was higher after MMRV as compared to MMR+V; however Klein et al. did not find a significantly increased risk with the MMRV vaccine. Pet. Ex. 19 at 2, 8; Pet. Ex. 21 at 2. Both studies showed that both MMRV and MMR+V "are associated with fever and seizure [seven] to 10 days after vaccination," but neither reported increase of seven fold, as testified to by Dr. Kinsbourne. Pet. Ex. 19 at 8; see also Pet. Ex. 21 at 2. When asked to identify the study that reported a seven-fold increase in seizures following the MMRV vaccination, Dr. Kinsbourne was unable to remember the name of the article. Tr. 105-07.

Next, Dr. Kinsbourne opined febrile seizures can lead to death in certain circumstances depending on the seizure threshold of the individual and risk factors. Tr. 84, 251; Pet. Ex. 13 at 3; Pet. Ex. 61 at 2-3. He explained that febrile seizures are "really common" and occur in two to five percent "of all children." Tr. 85. He testified that most are short and benign, but some (30%) may be prolonged, and thus, dangerous. Id. "In a healthy child and an uncomplicated setting[,] a simple febrile seizure would indeed not be considered potentially fatal." Pet. Ex. 61 at 3.

He testified that unobserved seizures "undoubtedly" occur and can cause death. Tr. 84-85; see, e.g., Pet. Ex. 18. He added that the risk of impaired respiration is less likely in a witnessed febrile seizure than in an unwitnessed seizure because interventions can occur when a seizure is witnessed. Pet. Ex. 61 at 3. Such lack of intervention "is especially true of unwitnessed seizures that occur during sleep." Id.; see also Tr. 80-81 (opining sleep increases the risk of seizures); Pet. Ex. 18 at 6. Dr. Kinsbourne maintained that "[t]he rarity of death due to a witnessed febrile seizure does not suggest that unwitnessed febrile seizures don't cause death." Pet. Ex. 61 at 3.

Dr. Kinsbourne explained that a family history of febrile seizures is "a risk factor for febrile seizures in a member of that family." Tr. 78. He added that "[a] family history makes it more likely that the seizure occurs in a given child." Tr. 103. Additionally, "[a] family history of febrile seizures is found in a disproportionate percentage of infants who die in a sudden unexpected death." Pet. Ex. 13 at 3.

For support, he cited Hesdorffer et al.[48] and argued they "proposed that children with [SUDC] who had a family history of febrile seizures had an increased risk of dying in a terminal seizure." Pet. Ex. 13 at 2 (citing Pet. Ex. 16 at 2). They examined 123 SUDC cases and found 31.7% had a personal history of febrile seizures, 18.7% had a first-degree family history of febrile seizures, 96.8% died during sleep and the death was unwitnessed, 73.9% were found in the prone position at death, and 75.6% had a terminal fever or illness symptoms within 48 hours before death. Pet. Ex. 16 at 5, 4-5 tbl.1. Of the 84 SUDC cases without a personal history of febrile seizure, 75.9% had a terminal fever or illness symptoms within 48 hours of death, 70.1% were found in the prone position at death, and 14.3% had a first-degree family history of febrile seizures. Id. at 6, 4-5 tbl.1. Hesdorffer et al. found that "[i]n children with SUDC and a history of [febrile seizure], terminal fever may increase the risk for an unwitnessed terminal seizure." Id. at 2. Dr. Kinsbourne acknowledged that this finding relates to a personal history of febrile seizures, and not a family history of febrile seizures. Tr. 103. Hesdorffer et al. could not "exclude the possibility in these unwitnessed deaths that among the 75.9% of children with terminal fever or illness symptoms but without a prior [febrile seizure], their first [febrile seizure] might have been a terminal event." Pet. Ex. 16 at 7.

Another article cited by Dr. Kinsbourne reported a similar conclusion related to children who had a history of febrile seizures. Crandall et al.[49] determined "[p]atients with febrile seizures are at [an] increased risk for sudden death." Pet. Ex. 72 at 2. The authors examined and interviewed 391 families where a child aged one to six died, and 264 were classified as SUDC. Id. at 4. Of these 264 cases, 181 did not have any seizure history, 76 had a febrile seizure history, and seven had an afebrile seizure history. Id. First- and second-degree family history of febrile seizures was found in 45 of 160 cases of SUDC without a personal seizure history. Id. at 5 tbl.1. Crandall et al. found SUDC cases with a personal history of febrile seizures were more likely to have a family history of seizures, both febrile and afebrile. Id. at 6. Additionally, 253 of 264 (95.8%) SUDC cases were found unresponsive during a sleep period and 173 of 211 (82%) were discovered in the prone position. Id. at 5. In 112 of 245 SUDC cases (45.7%), a terminal fever was reported. Id. Crandall et al. concluded their "findings implicate [febrile seizure] as a contributing factor or cause of death via a SUDEP-like process in some SUDC cases." Id. at 6. The authors, however, "speculate[d] that [febrile seizures] occur in some children without a known [febrile seizure] history." Id. at 7. They added, "[p]ostmortem evidence of terminal seizures is often absent or nonspecific . . . . Explained deaths attributed to asphyxia could include [febrile seizure] cases where the child remained prone . . . ." Id.

Dr. Kinsbourne also cited medical literature relating to SUDEP and found this literature can relate to SUDC, explaining "[SUDEP] literature suggests indirectly, not with certainty, that in SUDC, there is, indeed, a tendency for the child to have had a history of febrile seizures, . . .

[48] Dale C. Hesdorffer et al., Sudden Unexplained Death in Childhood: A Comparison of Cases with and Without a Febrile Seizure History, 56 Epilepsia 1294 (2015).

[49] Laura Gould Crandall et al., Potential Role of Febrile Seizures and Other Risk Factors Associated with Sudden Deaths in Children, 2 JAMA e192739 (2019).

either a personal history or family history of febrile seizures." Tr. 82-83, 256. Dr. Kinsbourne cited Devinsky,[50] who suggested that cases of SUDEP may occur after a seizure, usually a tonic-clonic seizure. Pet. Ex. 15 at 3. Findings that may be seen include bitten tongue or cheek and pulmonary edema. Id. at 2, 9 tbl.3. The finding of pulmonary edema was not explained. Devinsky also suggested that there may be impaired respiration following a seizure, which may be lethal and involve pulmonary dysfunction. Id. at 5, 6 tbl.2.

Kloster and Engelskjøn[51] examined risk factors and their role in SUDEP. Pet. Ex. 20 at 2. Of the 42 cases classified as SUDEP with no verified cause of death, 62% had pulmonary edema, 67% showed signs of a preceding seizure, 71% were found in the prone position at death, and 60% were found in bed "presumably dying before, during, or after sleep." Id. at 2, 4-5. The authors noted signs of seizures immediately before death included fresh bites, blood on the pillow, cyanosis,[52] and sounds associated with ongoing seizures. Id. at 3. "The prone position may cause obstruction of the nose and mouth due to pressure against the bed clothing." Id. at 5. The authors hypothesized that those who were found dead in bed may have died due to their positioning or due to sleep itself, which would implicated the respiration.[53] Id. at 6. Kloster and Engelskjøn noted, "[c]learly[] seizures play an important part in SUDEP, but some patients die without visible seizures," and thus, there is a "possibility that some of these deaths are unrelated or only indirectly related to epilepsy." Id. at 5.

Dr. Kinsbourne also cited Kinney et al. (2009) and Hefti et al., discussed in more detail above, which reported an association of sudden death, febrile seizures, hippocampal abnormalities, and sleep. Pet. Ex. 13 at 2 (citing Pet. Ex. 18); Pet. Ex. 61 at 3 (citing Pet. Exs. 27-28). Kinney et al. "suggest[ed] that simple febrile seizures may not be totally benign," and found a group of deaths characterized by sleep-related unwitnessed sudden death in the toddler in the prone position, individual/family history of febrile seizures, and hippocampal anomalies." Pet. Ex. 18 at 7. Based on the medical literature, Dr. Kinsbourne opined febrile seizures can be lethal in certain circumstances. Pet. Ex. 61 at 3.

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[50] Orrin Devinsky, Sudden, Unexpected Death in Epilepsy, 365 New Eng. J. Med. 1801 (2011).

[51] Robert Kloster & Torstein Engelskjøn, Sudden Unexpected Death in Epilepsy (SUDEP): A Clinical Perspective and a Search for Risk Factors, 67 J. Neurology Neurosurgery & Psychiatry 439 (1999).

[52] Cyanosis is "a bluish discoloration, especially of the skin and mucous membranes due to excessive concentration of deoxyhemoglobin in the blood." Cyanosis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=12098 (last visited Nov. 13, 2023).

[53] See also Pet. Ex. 17 (John Hewertson et al., Epileptic Seizure-Induced Hypoxia in Infants with Apparent Life-Threatening Events, 94 Pediatrics 148 (1994)) (explaining how epileptic seizures can be accompanied by episodes of hypoxia and apnea).

ii. Althen Prongs Two and Three

Dr. Kinsbourne opined the MMRV vaccine N.A. received on June 23, 2016 triggered a fever and an unobserved seizure that caused her death on June 30, 2016. Tr. 76-78; Pet. Ex. 13 at 3-4; Pet. Ex. 61 at 2-3. He summarized that N.A. was at an increased risk for sudden unexplained death because her family history of febrile seizures put her at risk for a febrile seizure, her hippocampal abnormalities made her more susceptible to seizure generation, and sleep lowered her seizure threshold. Pet. Ex. 61 at 2. Because of this triad of risk factors, she was "vulnerable to the febrile seizure risk inherent in MMRV, to which she succumbed." Id.

He explained N.A. received her MMRV vaccine on June 23, and seven days later, on June 30, she developed a fever. Tr. 79-80; Pet. Ex. 13 at 1-3. Because N.A.'s fever was within the risk interval following an MMRV vaccination, he opined "the presumption is that [the fever] was an MMRV fever." Tr. 77; see also Pet. Ex. 61 at 3. Dr. Kinsbourne acknowledged that N.A.'s fever was a low-grade fever, and that Mrs. Anklam did not take N.A.'s temperature. Tr. 92-93. He agreed that that literature associates febrile seizures with a certain threshold of temperature (about 102°F), but he opined that a temperature under 100°F can trigger a seizure depending on the individual's seizure threshold. Tr. 107-08. However, he agreed that a temperature of less than a 100°F "would not be sufficient" to cause a seizure in most people. Tr. 107. There would have to be "some genetic trait" to cause "relatively low seizure threshold." Id. He also agreed that N.A.'s seizure threshold was unknown. Tr. 108.

He "assume[ed] that when [N.A.] had the seizure . . . , her temperature had gone considerably higher." Tr. 94. "In other words, it was the beginning of a fever engendered by the vaccination." Id.

Dr. Kinsbourne next opined that this fever caused by her MMRV vaccination led to an unobserved seizure that caused N.A.'s death due to her family history of seizures, prone position on death, and evidence of pulmonary edema and hippocampal abnormality on autopsy. Tr. 76-78; Pet. Ex. 13 at 3-4.

As noted above, one of N.A.'s brother has a history of febrile seizures. Tr. 78, 98; Pet. Ex. 13 at 1-3. Dr. Kinsbourne opined "[a] family history of febrile seizure is found in a disproportionate percentage of infants who die a sudden unexpected death." Pet. Ex. 13 at 3.

Second, N.A. was found in the prone position on death, and Dr. Kinsbourne believed she was likely already unconscious when she got into this position. Tr. 86; Pet. Ex. 61 at 2. He added that this position would make it hard for her to breathe. Tr. 85-86. The medical examiner "could not explain why [N.A.] remained face down" and "cautioned that a one-year-old who is lying face down is capable of turning to the side if she becomes short of breath." Pet. Ex. 13 at 2 (citing Pet. Ex. 6 at 1); see also Pet. Ex. 61 at 2; Tr. 96. Dr. Kinsbourne agreed that children at one year of age "are well able to move their head sideways if the circumstances require it, which she clearly didn't have that ability." Tr. 86.

Additionally, Dr. Kinsbourne opined this position at death was "suggestive of terminal seizure activity;" "the configuration of the body in rigor mortis was unusual, less like an infant

death by asphyxia than death during a seizure." Pet. Ex. 13 at 2-3. He noted that although the medical examiner diagnosed death by asphyxia, the manner of death was undeterminable. Id. at 2; see Pet. Ex. 6 at 1 ("[N.A.] died of asphyxia. . . . The manner of death is undeterminable.").

And third, because pulmonary edema was found on autopsy, Dr. Kinsbourne opined that N.A.'s respiratory system likely was unable to maintain normal functioning for long enough for N.A. to survive, and lying on her face would have made it difficult to breathe. Tr. 85-86; Pet. Ex. 13 at 2. However, medical literature referenced by Dr. Kinsbourne does not show that the finding of pulmonary edema is specific to a seizure or evidence of a seizure. Although Devinsky noted "[s]eizure can cause pulmonary edema" and that "[p]ulmonary edema is the most common autopsy finding," Devinsky failed to explain how a finding of pulmonary edema is specific to a seizure. Pet. Ex. 15 at 5, 6 tbl.2. Kloster and Engelskjøn observed the incidence of pulmonary edema in SUDEP cases, but they did not state that it was a sign of seizure. Pet. Ex. 20 at 3. And they did not attribute pulmonary edema specifically to seizures. Id. Harowitz et al. described pulmonary edema as a non-specific finding. Pet. Ex. 74 at 5.

At the hearing, Dr. Kinsbourne testified that his findings regarding N.A.'s hippocampal abnormalities are based on Dr. Miller's opinions, and he acknowledged the medical examiner who conducted the autopsy found no abnormalities. Tr. 91-92; see also Pet. Ex. 13 at 2. Dr. Kinsbourne opined the hippocampal abnormality Dr. Miller described would double N.A.'s risk of seizure. Tr. 83. If N.A. did not have the hippocampal abnormality, Dr. Kinsbourne "would regard the evidence [in favor of a seizure the night of June 30, 2016] as less strong, but still easily strong enough." Id. He maintained "that more likely than not, N.A. did die because of the MMRV [vaccine] causing a febrile seizure which then precipitated her death as described" even without a hippocampal abnormality. Tr. 83, 102.

Overall, Dr. Kinsbourne found "the presumption that there was a seizure [was] strong." Tr. 84. "[A]nd if she had a seizure the possibility or the probability that it cause[d] her death [was] also strong, considering [] that there [were] no other factors in evidence that could have caused her death." Id. He opined it was "impossible" to know how long N.A.'s inferred seizure lasted. Tr. 85. He also acknowledged that N.A. had no history of seizure but hypothesized that "if N.A. had survived, she might have had the seizures subsequently or not." Tr. 103.

In response to Dr. Lidov's arguments that N.A.'s absence of tongue biting was evidence against the existence of an unwitnessed seizure, Dr. Kinsbourne explained "[t]he absence of a lacerated tongue at [N.A.'s] autopsy is not useful criterion of whether a seizure occurred." Pet. Ex. 61 at 2 (citing Pet. Ex. 28 at 6 tbl.2). Compare Pet. Ex. 20 at 3 (noting "fresh bites" to be a sign of a seizure), and Pet. Ex. 15 at 2, 9 tbl.3 (finding evidence of a seizure to include bitten tongue or cheek), with Pet. Ex. 72 at 7 (indicating tongue biting is an "infrequent" finding), and Pet. Ex. 74 at 5 ("In young children, seizures may lack classic signs (e.g., . . . tongue-biting), making diagnosis more difficult."). He agreed with Dr. Lidov that "there is no direct scientific proof" a seizure occurred; however, he stressed that "there is ample circumstantial evidence [N.A.] died in a seizure." Pet. Ex. 61 at 2.

Regarding the length of N.A.'s seizure, Dr. Kinsbourne agreed that most febrile seizures are short and benign, but he explained if they are prolonged, they are more dangerous. Tr. 85.

Dr. Kinsbourne testified that it is "impossible to say how long N.A.'s inferred seizure was, but unfortunately, she died, and there was no other imaginable reason why she might have died." Id.

Dr. Kinsbourne maintained there was no evidence of alternative causation. Pet. Ex. 13 at 3; Pet. Ex. 61 at 3. In response to Dr. McCusker's argument that N.A. had a viral respiratory infection that would have explained N.A.'s fever and blocked N.A.'s airway, Dr. Kinsbourne opined that no infection was diagnosed and the autopsy did not reveal an obstructed airway. Pet. Ex. 61 at 3. He added that any fever N.A. may have had in the week leading up to her MMRV vaccination "was evidently insufficient to provoke a seizure[] because it did not in fact do so." Id. Lastly, he opined "[t]he fever at the time of [N.A.'s] death can more directly be attributed to the MMRV vaccination." Id.

As for the temporal association between vaccination and seizure, Dr. Kinsbourne emphasized that N.A. had an elevated risk of seizure because she received her MMRV vaccination seven days prior to her death. Pet. Ex. 61 at 1-2.

3. Respondent's Expert, Dr. Hart G.W. Lidov, M.D., Ph.D.[54]

a. Background and Qualifications

Dr. Lidov is a board-certified neuropathologist and pediatric neurologist, licensed in Massachusetts. Resp. Ex. E at 1-2; Resp. Ex. P at 6. He obtained his B.A. in Biophysics, Ph.D. in Anatomy, and M.D. from Johns Hopkins before completing a pediatric internship at Massachusetts General Hospital and residencies in pediatrics, neurology, neuropathology, and anatomic pathology at Massachusetts General Hospital, National Hospital Queens Square in London, UK, and Brigham and Women's Hospital. Resp. Ex. P at 1. He held clinical fellowships in pediatrics, neurology, and pathology and neurology at Harvard Medical School and has been a Professor in pathology and neurology at Harvard Medical School for almost 20 years. Id. at 1-2. Since 1991, he has been a staff Neuropathologist at Boston Children's Hospital and Brigham and Women's Hospital. Id. at 2. He "routinely see[s] surgical neuropathology cases from these hospitals, and autopsy examinations of the [central nervous system], as well as consultations." Resp. Ex. E at 2. Dr. Lidov has authored or co-authored over 100 publications. Resp. Ex. P at 8-16.

b. Opinion

i. Althen Prong One

Dr. Lidov opined that Petitioners' theory that N.A.'s MMRV vaccination caused a fatal unwitnessed seizure was unlikely. Tr. 141-43. He explained that febrile seizures are uncommon and rare, and "a febrile seizure following a vaccination by itself is an extremely unlikely event." Tr. 116-17 (citing Pet. Ex. 19). He did agree that the MMRV vaccine increases the risk of fevers and seizures in the period of seven to 10 days post-vaccination. Tr. 148. However, based on his personal experience and review the literature, Dr. Lidov opined that a first febrile seizure is not

[54] Dr. Lidov submitted three expert reports and testified at the hearing. Resp. Exs. E, I, M; Tr. 3.

known to be fatal. Tr. 118-23; Resp. Ex. E at 4-5; Resp. Ex. M at 1. Further, since febrile seizures are the most common form of seizures in children, he expected that if there was an increase in mortality associated with an initial febrile seizure, it would probably be reported in the literature. Resp. Ex. E at 5; see also Resp. Ex. I at 13 ("If simple febrile seizures had the potential to be fatal, there should be reports, likely many reports . . . .").

For support, he cited Byard,[55] who stated that death during febrile seizures was rare. Resp. Ex. E at 5 (citing Resp. Ex. E, Tab 1 at 2). Shinnar and O'Dell[56] stated "[t]he morbidity and mortality associated with febrile seizures is extremely low," and "[e]ven cases of febrile status epilepticus have shown almost zero mortality." Id. (quoting Resp. Ex. E, Tab 3 at 5); see also Resp. Ex. E, Tab 7 at 3 ("The mortality of febrile status epilepticus in recent series is extremely low.");[57] Resp. Ex. U at 3 ("The mortality associated with febrile seizures is extremely low.");[58] Resp. Ex. L at 2 (noting "the absolute risk of death [from febrile seizure] [is] [] very low").[59] Dr. Lidov also cited Leung and Robson,[60] who similarly reported "[c]hildren with febrile seizures have no increased risk of mortality." Resp. Ex. E at 5 (quoting Resp. Ex. E, Tab 4 at 4 (internal citations omitted)).

Dr. Lidov was not persuaded by Petitioners' literature. Tr. 119-20 (citing Pet. Exs. 70-71); see also Resp. Ex. E at 5 (citing Pet. Ex. 70). Dlouhy et al., for example, noted "no documented case of febrile seizure-induced death has been reported" in SUDC, "[a]lthough some cases of [SUDC] cases have a history of febrile seizures." Pet. Ex. 70 at 2. Dr. Lidov also explained that the Dlouhy et al. case report involved a child with a prior history of multiple complex seizures prior to the terminal event. Tr. 119 (citing Pet. Ex. 70 at 2). Based on this history, she would not be classified as SUDC, but as SUDEP. Id. (citing Pet. Ex. 70 at 2).

Further, Dr. Lidov opined that since N.A. did not have a history of prior seizures, and her "death [was] unwitnessed, [] the occurrence during a febrile seizure [was] only a supposition." Resp. Ex. E at 5 (citing Pet. Ex. 70 at 2).

Dr. Lidov also disagreed that the case report by Myers et al. was relevant, opining that the child's death described in Myers et al. was not caused by a fatal febrile seizure but instead

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[55] Roger W. Byard, Sudden Death in the Young (3d ed. 2010). Three non-consecutive pages from this textbook were filed.

[56] Shlomo Shinnar & Christine O'Dell, Febrile Seizures, 33 Pediatric Annals 395 (2004).

[57] Shlomo Shinnar & Tracy A. Glauser, Febrile Seizures, 17 J. Child Neurology S44 (2002).

[58] 1 Shlomo Shinnar, Febrile Seizures, in Swaiman's Pediatric Neurology 790 (Kenneth F. Swaiman et al. eds., 5th ed. 2012).

[59] Maitreyi Mazumdar, Febrile Seizures and Risk of Death, 372 Lancet 429 (2008).

[60] Alexander K.C. Leung & W. Lane M. Robson, Febrile Seizures, 21 J. Pediatric Health Care 250 (2007).

reflected the child's complex chromosomal abnormality. Tr. 119-20 (citing Pet. Ex. 71 at 1). The child had a chromosomal disorder with "dysmorphic features, bilateral cleft palate, short webbed neck, congenital heart disease . . . , and severe bilateral bronchomalacia." Pet. Ex. 71 at 3. Brain magnetic resonance imaging ("MRI") was abnormal. Id. She had "hypotonia from birth and global developmental delay." Id. Although the child presented to the hospital after febrile status epilepticus, she did not experience sudden death until two days later, during video EEG monitoring. Id. The authors suggested that the physiologic changes prior to death may be similar to "some rare cases of adults who have experienced [SUDEP]." Id. at 2. N.A. did not have epilepsy.

Dr. Lidov was also not persuaded by Petitioners' reliance on Crandall et al. Tr. 120 (citing Pet. Ex. 72). There, the researchers collected interviews of family members who had voluntarily registered with the SUDC Foundation.[61] Pet. Ex. 72 at 2. In the SUDC group, 87 of 241 (36.1%) reported a family history of febrile seizures, and 41 of 241 (17%) reported both a case and family history. Id. at 5. Information was obtained from "[d]etailed demographic and interview histories." Id. at 4. "No independent medical record or autopsy review was performed." Id. at 3. Due to the lack of such more specific information, Dr. Lidov did not find the study persuasive. Tr. 120.

On cross-examination, Dr. Lidov agreed that not all seizures are witnessed and some occur during sleep. Tr. 146-47. He also agreed that seizures can cause death, specifically generalized tonic-clonic seizures and focal seizures. Tr. 147, 156. He opined that the literature, specifically articles authored or co-authored by Dr. Kinney, hypothesizes that an unwitnessed seizure can cause SUDC. Id. But he opined that articles related to SUDEP have only raised the possibility, which is "unproven," that unwitnessed seizures can lead to death. Tr. 147-48.

Regarding Petitioners' assertion that the presence of hippocampal abnormalities is evidence that supports Petitioners' theory, Dr. Lidov disagreed. Resp. Ex. E at 5-7; Resp. Ex. I at 13. Any association between febrile seizures and hippocampal abnormalities, according to Dr. Lidov, is not evidence of a causal mechanism. Resp. Ex. E at 4-5; Resp. Ex. I at 13. He explained that the literature noted an association, but never showed causality, despite Dr. Miller's assertions. Resp. Ex. E at 5-7 (citing, e.g., Pet. Exs. 18, 26-29). Dr. Lidov contended that Petitioners are proposing a theory that "is at most 'conceivable,' or 'cannot be proven to be utterly impossible.'" Resp. Ex. I at 13. Dr. Lidov found Dr. Kinney's hypothesis that the mechanism in SUDC cases is an epilepsy-like mechanism may be plausible, but it is unproven. Tr. 157; see Pet. Ex. 29 at 13.

Dr. Lidov agreed that a family history of febrile seizures is a risk factor for febrile seizures, but noted it is because of a genetic component. Tr. 139-40; see also Resp. Ex. E, Tab 7 at 2 tbl.1 (noting first-degree relative with history of febrile seizures as a risk factor for first febrile seizure); Resp. Ex. E, Tab 4 at 2 (same). Even though a family history of febrile seizures increases the risk of having a febrile seizure, Dr. Lidov maintained "it [does not] make it a likely event." Tr. 140; see also Resp. Ex. I at 13 (explaining "all children are at some risk," but "this does not prove that [a seizure] occurred").

[61] Of note, Dr. Orrin Devinsky was a named author on this paper.

He opined that Petitioners suggest that a febrile seizure can cause death and relied upon literature noting an association of a family or personal history of febrile seizures with SUDC. Tr. 144-45. He concluded that any association is not causal and in fact, a history of febrile seizure is a marker for a genetic abnormality. Tr. 145. And these genetic abnormalities can explain SUDC via a different mechanism. Id.

ii. Althen Prongs Two and Three

Dr. Lidov opined Petitioners' theory was weak and unlikely here. Tr. 141; Resp. Ex. E at 8-9. He found that more likely than not, N.A.'s vaccination was unrelated to her death. Resp. Ex. E at 9. Additionally, he found no evidence to support the assertion that more likely than not, N.A. died of a fatal first febrile seizure. Resp. Ex. I at 12.

Dr. Lidov concluded there was "no evidence of a seizure, febrile or otherwise," no evidence N.A. was febrile, and even if she was febrile, there was evidence that it was antecedent to her vaccination. Tr. 141-42. Next, he explained there is no literature to support a finding of a first fatal febrile seizure. Id.; see also Resp. Ex. I at 12. Moreover, the literature reports hippocampal abnormalities in children without a history of seizures. Tr. 142. He opined the probability of this factor of Petitioners' theory was "more reasonable," however, he found it was a "low probability of indicating seizures." Id. Lastly, he opined the MMRV vaccine "was not in any way responsible for [N.A.'s] death." Tr. 144.

Dr. Lidov opined there was no evidence that N.A. had a seizure at the time of her death for numerous reasons. Resp. Ex. E at 4; see also Tr. 117; Resp. Ex. I at 12-14; Resp. Ex. M at 1. First, N.A. had no history of seizures or any history of febrile responses following any previous vaccinations. Resp. Ex. E at 4. Second, there was no report of tongue biting on autopsy, despite evidence of deciduous dentition. Id. He noted the lack of physical evidence (tongue biting, disrupted bed clothing) does not prove N.A. did not have a seizure, but would be strong evidence in favor of a seizure if this evidence was present. Tr. 117.

Third, N.A. only had "a very low fever," which "argues [] against the idea of [N.A.] having had a febrile seizure" because her temperature did not reach the threshold seen in fever-induced seizures. Tr. 117-18; see also Resp. Ex. E at 8 (noting a fever-induced seizure typically requires a significant fever of around 103°F); Resp. Ex. E, Tab 4 at 2 ("The most significant risk factor for the development of a first febrile seizure is the height of the temperature; the higher the temperature, the higher the likelihood of a febrile seizure."). Because N.A. had experienced low-grade fevers prior to the night of June 30 but had never had a seizure, Dr. Lidov argued that it is "less likely" that N.A.'s response to the low-grade fever on June 30 would be a seizure. Tr. 140-41; see also Resp. Ex. E at 8. Additionally, because N.A. had low-grade fevers since June 19, prior to her MMRV vaccination, Dr. Lidov found "no basis for presuming her vaccination[] [was] a necessary cause." Resp. Ex. E at 8.

Fourth, Dr. Lidov did not find N.A.'s family history of febrile seizures in her brother to be persuasive evidence that she had a seizure. Tr. 118. Lastly, Dr. Lidov did not find the fact that N.A. was found in the prone position to be evidence that she died of a seizure. Tr. 138-39.

He found it indicated that N.A. was unconscious at the time of her death but did not provide evidence of the cause of death. Tr. 138-39, 156. Additionally, he asserted it could indicate other processes that result in the prone position. Tr. 155. Given Dr. Lidov's experience, and his review of the literature, he found no evidence of a first febrile seizure being fatal. Tr. 123, 137, 141-42.

Dr. Lidov disagreed with Dr. Miller's brain abnormality findings and opined "the autopsy brain slides were completely [] normal for her age." Tr. 125; see also Resp. Ex. E at 3 (noting "the brain regions sampled show[ed] no definite or diagnostic abnormalities"); Resp. Ex. I at 2-12 (detailing his disagreements with Dr. Miller over the brain slides and findings); Resp. Ex. M at 1-2 (maintaining bilamination and dispersion were not present on N.A.'s slides). He found the photomicrographs "simply [did] not show bilamination at all and that there [were] no other abnormalities in the hippocampus." Tr. 136; see also Resp. Ex. E at 8. He also found it "unclear" how cell loss in the inferior olivary bears on this case as it is not a source of seizures. Tr. 136.

Specifically, Dr. Lidov found no evidence of a subtle depletion of the large neurons from each inferior olivary nucleus and no evidence of bilamination. Tr. 125; Resp. Ex. E at 3, 8. In his expert reports and during the hearing, Dr. Lidov detailed what a normal dentate gyrus and bilamination look like, relying on photographs from the literature, and using those, he explained why N.A. exhibited no hippocampal abnormalities. See Tr. 126-34; Resp. Ex. E at 3, 8; Resp. Ex. I at 5-9 (citing Pet. Exs. 26, 29; Resp. Ex. I, Tab 2;[62] Resp. Ex. I, Tab 5;[63] Resp. Ex. I, Tab 8).[64] Dr. Lidov also detailed his findings as to the inferior olivary. See Tr. 136-37; Resp. Ex. I at 9-12.

He opined that Dr. Miller's photomicrographs of N.A.'s dentate gyrus were at a higher magnification and not the same magnification as the photographs in the literature. Tr. 134. By using a higher magnification, Dr. Lidov testified, "you can find areas like this in normal dentate gyruses and in dentate gyruses of children who've died of lots of different diseases." Id. He further explained that a close up, cropped photograph does not show the entire field. Tr. 135. Overall, he found Dr. Miller's photomicrographs "not convincing for bilamination." Id.; see also Resp. Ex. I at 12

Further, in a supplemental report, Dr. Lidov noted "the significance attributed to the presence of hippocampal malformations may be moot" as recent studies have suggested such findings occur more frequently in the general population. Resp. Ex. M at 2; see, e.g., Resp. Ex.

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[62] Ingmar Blümcke et al., Towards a Clinico-Pathological Classification of Granule Cell Dispersion in Human Mesial Temporal Lobe Epilepsies, 117 Acta Neuropathology 535 (2009).

[63] Carolyn R. Houser, Granule Cell Dispersion in the Dentate Gyrus of Humans with Temporal Lobe Epilepsy, 535 Brain Rsch. 195 (1990).

[64] Alexandre Valoota da Silva et al., Dysmorphic Neurons in Patients with Temporal Lobe Epilepsy, 1072 Brain Rsch. 200 (2006).

K at 2; Resp. Ex. I, Tab 1 at 18.[65] Thus, "their presence or absence is of no established significance." Resp. Ex. M at 2. He cited Dr. Miller's first expert report, which stated,

> [f]or completeness I must point out that I and some colleagues here at the University of Missouri School of Medicine have been studying this very issue of dentate gyrus dysplasia, and we have found that it is very common in the general autopsy population at all ages and with all sorts of causes of death [].

Pet. Ex. 22 at 7.

Additionally, Dr. Lidov referenced the SUDCRRC investigation and the fact that they did not find any brain abnormality confirmed his opinions that N.A. did not have any brain abnormalities. Tr. 144. Dr. Lidov explained that the SUDCRRC neuropathologist would have focused on brain abnormalities, a focus of interest in their group. Tr. 154. Additionally, he testified that Dr. Devinsky, the principal investigator of the SUDCRRC report, is also an author in many of the articles filed herein on the subject of brain abnormalities in children. Tr. 153-55; see, e.g., Pet. Exs. 15, 72, 74.

In summary, Dr. Lidov agreed that N.A. fell into the SUDC category. Tr. 138; Resp. Ex. E at 4. He opined that her death was unexplained, stating "[w]e do not understand why" N.A. died. Tr. 138. Speculative causes include genetic abnormalities and cardiac arrhythmia. Id.; see also Resp. Ex. I at 15. However, Dr. Lidov concluded that it is "very unlikely" that N.A. had a febrile seizure. Tr. 137. He disagreed that N.A. had any brain abnormalities. Id. And he opined the literature does not support Petitioners' theory that N.A. had a fatal febrile seizure. Id. Lastly, Dr. Lidov opined that more likely than not, N.A.'s vaccination was unrelated to her death. Resp. Ex. E at 9.

4. Respondent's Expert, Dr. Sara O. Vargas, M.D.[66]

a. Background and Qualifications

Dr. Vargas is a pathologist with board certifications in anatomic pathology, clinical pathology, and pediatric pathology. Resp. Ex. C at 2. She received her A.B. from Harvard University and an M.D. from the University of Vermont College of Medicine. Resp. Ex. Q at 1. She then completed a residency in anatomic and clinical pathology and fellowship in pulmonary pathology at Brigham and Women's Hospital and a pediatric pathology fellowship at Children's Hospital in Boston, Massachusetts. Id.; Tr. 161. Dr. Vargas is an associate professor at Harvard Medical School and a staff pathologist at Children's Hospital and Brigham and Women's Hospital. Resp. Ex. Q at 1-2; Resp. Ex. C at 2. As a pathologist, she "practice[s] surgical pathology, cytopathology, postmortem examinations, and consultative diagnostic services."

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[65] Achira Roy et al., Hippocampal Granule Cell Dispersion: A Non-Specific Finding in Pediatric Patients with No History of Seizures, 8 Acta Neuropathologica Commc'ns 1 (2020).

[66] Dr. Vargas submitted three expert reports and testified at the hearing. Resp. Exs. C, J, N; Tr. 3.

Resp. Ex. C at 2. She also reviews autopsies for Robert's Program, "a multidisciplinary group that investigates sudden unexpected death in infancy and in childhood," similar to SUDCRRC. Tr. 164-65, 167. Dr. Vargas has authored or co-authored over 200 publications. Resp. Ex. Q at 18-41.

b. Opinion

Dr. Vargas opined N.A. "died of [SUDC] in the setting of a viral respiratory tract infection," with "no evidence that immunizations caused, or contributed in any way to [] [N.A.'s] death." Resp. Ex. C at 8; see also Resp. Ex. J at 1, 4.

i. Althen Prong One

Dr. Vargas opined there is no evidence that vaccination can cause SUDC via a seizure. Tr. 168; Resp. Ex. J at 1-2 (finding "no evidence that vaccinations are associated with any increased risk of SIDS/SUDC or that they 'potentiate' SIDS/SUDC"). Dr. Vargas testified that certain vaccinations protect against forms of sudden death. Tr. 168. Varicella, for example, "protects against varicella and therefore protects against the fatal complication of that which can include fatal pneumonia, fatal superimposed bacterial pneumonia on a viral pneumonia, or sometimes from the skin lesions[] you can get a superimposed bacterial infection[] [] that can enter the bloodstream and cause death." Tr. 168-69.

Dr. Vargas also "disagree[d] strongly with [Petitioners'] theory that the large majority of SIDS and SUDC are caused by a seizure," regardless of the presence of a hippocampal abnormality. Tr. 179. She opined that the hippocampal abnormality described in cases of SIDS, SUDC, and SUDEP "is a nonspecific finding" seen in many cases. Resp. Ex. J at 3; see also Tr. 178-79. "Although it is present at increased rates in patients with epilepsy history, it is unclear whether the hippocampal malformation might be a cause of seizure, a consequence of seizure, two separate consequences of another abnormality (e.g., genetic), or other." Resp. Ex. J at 3 (citing Resp. Ex. J, Tab 5 at 8-9).[67] Additionally, she noted there is no evidence that such malformations "cause death, no evidence that fever induces them to cause death, nor any evidence that vaccination induces them to cause death." Id. Thus, Dr. Vargas argued the presence of a hippocampal abnormality does not automatically classify a case as SUDC without a cause or explanation. Tr. 178.

In support of her opinions, Dr. Vargas cited several papers. McGuone et al. examined 20 SUDC cases and found 12 had a history of febrile seizures, 85% died during apparent sleep, and 80% were in the prone position. Resp. Ex. J, Tab 5 at 1. The authors concluded that any "significance and specificity of hippocampal findings [was] unclear" because abnormalities in the dentate gyrus were found in unexplained and explained deaths. Id. at 1, 8-9. Thus, the "hippocampal findings may be a result of seizures, a contributor to seizures, an unrelated phenomenon, or a normal anatomic variant in children." Id. at 9.

[67] Declan McGuone et al., Neuropathologic Changes in Sudden Unexplained Death in Childhood, 79 J. Neuropathology & Experimental Neurology 336 (2020).

Abdel-Mannan et al.[68] defined a definite case of SUDEP as "[s]udden, unexpected, witnessed or unwitnessed, non-traumatic and non-drowning death, occurring in benign circumstances, in an individual with epilepsy, with or without evidence for a seizure and excluding documented status epilepticus in which postmortem examination does not reveal a cause of death." Resp. Ex. J, Tab 1 at 2. Dr. Vargas explained the mechanism of death in SUDEP is unknown. Resp. Ex. J at 3 (citing Resp. Ex. J, Tab 1 at 1). There is also no evidence that fevers can trigger SUDEP. Id. Dr. Vargas explained that for SUDEP, it is postulated that abnormalities of ion channels in the brain and heart may render individuals predisposed to seizures and sudden cardiac arrest. Id. (citing Resp. Ex. J, Tab 1 at 7).

Dr. Vargas agreed the MMRV vaccination causes fevers and sometimes causes seizures, and this risk of seizure peaks at seven to 10 days post-vaccination. Tr. 181-82. When asked whether death could occur when "a child [] sleeping on the[ir] stomach [] [loses] consciousness due to a seizure," Dr. Vargas testified "[p]robably." Tr. 185. She explained, however, that death from a first febrile seizure is rare. Tr. 180.

She also noted fevers caused by viral infections can trigger seizures. Tr. 184. And seizures can lead to injuries, such as tongue biting, falls, and a compromised respiratory tract due to aspiration of material. Tr. 184-85.

ii. Althen Prongs Two and Three

Dr. Vargas agreed N.A.'s death is best classified as SUDC. Resp. Ex. C at 5; Resp. Ex. J at 4; Tr. 169. Although there are aspects of N.A.'s death that resemble SIDS, Dr. Vargas opined N.A.'s death does not qualify as SIDS. Resp. Ex. C at 5; see also Tr. 163-64 (testifying there is a "strict age cut-off" at "one year of age"). She also opined that N.A. did not have epilepsy or SUDEP, and even if she had a history of epilepsy, Dr. Vargas found no evidence that a vaccine-induced fever could have caused death in such scenario. Resp. Ex. J at 3.

Next, Dr. Vargas opined that there is no evidence that N.A. had a febrile seizure. Resp. Ex. C at 6-7; Tr. 175. She noted N.A. had no history of seizures and no seizure was observed on the night of her death. Resp. Ex. C at 6. N.A.'s fevers around the time of her death were only "low-grade, lower than characteristically observed with febrile seizures." Id.; see also Tr. 175-76. Additionally, Dr. Vargas found N.A.'s autopsy showed no evidence of seizure activity. Resp. Ex. C at 6. For example, there was no evidence of tongue-biting, which is a finding Dr. Vargas found typical with a suspected seizure. Id. at 7. Dr. Vargas found "[t]he fact that the medical examiner did not describe or sample [N.A.'s] tongue may reflect a lack of any substantial degree of suspicion for seizure on the part of the medical examiner." Id.

She disagreed with Petitioners' experts' arguments that a history of seizures in N.A.'s brother was evidence that N.A. had a seizure. Resp. Ex. C at 7. While Dr. Vargas agreed that "[s]eizures can be familial," she disagreed that "[h]aving a single family member with seizures . .

[68] Omar Abdel-Mannan et al., A Systematic Review of Sudden Unexpected Death in Epilepsy (SUDEP) in Childhood, 90 Epilepsy & Behavior 99 (2019).

. automatically confer[s] seizure susceptibility." Tr. 176; Resp. Ex. C at 7. Additionally, N.A. did not exhibit a history of seizures or developmental issues that were seen in her brother. Resp. Ex. J at 2; Tr. 176-77. Thus, Dr. Vargas opined any link between N.A.'s death and her brother's seizures "[was] tenuous at best" and "probably negligible." Resp. Ex. J at 2; Tr. 177.

Dr. Vargas questioned Dr. Kinsbourne's opinions that "the configuration of the body in rigor mortis was unusual, less like an infant death by asphyxia than death during a seizure." Resp. Ex. C at 7 (quoting Pet. Ex. 13 at 2). She responded that Dr. Kinsbourne "provide[d] no explanation for what was 'unusual' about the rigor mortis, or why the configuration would indicate death due to seizure." Id. Additionally, the autopsy did not mention a particular body configuration that was "unusual" and rigor mortis, as Dr. Vargas explained, "is a natural and expected phase of postmortem change, and it is not in any way an indication of seizure." Id.

With regard to the prone position on death, Dr. Vargas agreed this position is a common position in patients with SIDS or SIDS-like death and "it supports some of the mechanisms . . . proposed in SIDS." Tr. 176. And for the disagreement as to the presence of a hippocampal abnormality in N.A., Dr. Vargas noted the presence of such abnormality "[was] not critical to [her] opinion that [N.A.'s] death was not caused by vaccination nor by fever." Resp. Ex. J at 3.

Dr. Vargas reviewed the report from SUDCRRC. Resp. Ex. N at 1-2. She noted the SUDCRRC did not find vaccination, fever, or seizure to be a cause of N.A.'s death. Id. The report concluded cause of death was unexplained sudden death with an undetermined manner of death. Id. at 2 (citing Pet. Ex. 77 at 9). Additionally, SUDCRRC conducted a genetic analysis and identified no known or expected pathogenic variants.[69] Id. (citing Pet. Ex. 77 at 8); see also Pet. Ex. 80 (genetics report). Based on the lack of any genetic abnormalities, Dr. Vargas opined that N.A. "had a little low risk" of seizures given the fact that the SUDCRRC did not identify genetic susceptibility to seizures. Tr. 177.

Regarding the autopsy, Dr. Vargas reviewed the 12 autopsy slides and had several opinions.[70] Resp. Ex. C at 3-6; Tr. 171-72. First, she opined that there were no pathologic features shown in the heart tissue. Resp. Ex. C at 4.

Second, Dr. Vargas found some of N.A.'s organs weighed more than what would be expected in a child N.A.'s age. Resp. Ex. C at 3 (citing Resp. Ex. C, Tab 1).[71] She noted that the lungs stood out as heavy compared to other organs. Id. at 5-6; Tr. 172. Dr. Vargas agreed

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[69] Dr. Vargas hypothesized the role of genetics in N.A.'s death in an expert report, prior to the filing of the genetic testing results from SUDCRRC. See Resp. Ex. J at 1-2.

[70] For Dr. Vargas' findings on the microscopic slides, see Resp. Ex. C at 4.

[71] J.M. Coppoletta & S.B. Wolbach, Body Length and Organ Weights of Infants and Children: A Study of the Body Length and Normal Weights of the More Important Vital Organs of the Body Between Birth and Twelve Years of Age, 9 Am. J. Pathology 55 (1933). Only one chart from the article was filed.

with the medical examiner that there was inflammation in the submucosa of the upper airway but opined the inflammation chronic, not minimal, because it was well developed and lymphoid follicles were seen. Tr. 171. She also testified there was inflammation in the lower respiratory tract in the lungs with mild expanded lymphoid tissue. Tr. 172. Additionally, she agreed with the medical examiner's finding of scatter macrophages in the alveoli; however, she did not find pulmonary edema present. Tr. 172, 188-89.

Based on the autopsy and other evidence, Dr. Vargas opined it was "unlikely that 'asphyxia' described the cause of death accurately or fully." Resp. Ex. C at 5. She explained "[a]sphyxia, by definition, indicated a lack of oxygen," and "[w]hen death is attributed to 'asphyxia' it usually indicated a blockage of air [] by a physical object." Id. "[N]atural diseases [] may lead to a deficiency of oxygen as the mechanism of death," but the term "asphyxia" is not applied. Id. She opined N.A. "had no obvious entanglement in bedding, no unsafe co-sleeping arrangement, and no apparent foul play to indicate asphyxiation as a sole cause of death." Id. She also agreed healthy one-year-olds "are expected to be able to turn their heads during periods of sleep to avoid suffocation." Id.

Regarding the cause of death, Dr. Vargas testified that there were many possible causes of death, including occult infection, cardiac arrhythmia, and failure to autoresuscitate. Tr. 180. On cross-examination, Dr. Vargas noted that these possible causes of N.A.'s death did not reach the level of more likely than not. Tr. 182-83. However, she opined that each were more likely to cause death than a febrile seizure. Tr. 185-86.

Dr. Vargas opined that "the most likely explanation for [N.A.'s] fevers was a virus." Resp. Ex. C at 5; see also Resp. Ex. J at 3. N.A. had low-grade fever beginning on June 19, 2016, which pre-dated her MMRV vaccination on June 23, 2016, and thus, it could not have been caused by vaccination. Resp. Ex. C at 5 (citing Pet. Ex. 5 at 5); Tr. 174; Resp. Ex. J at 3. Dr. Vargas opined N.A. had "chronic lymphoplasmacytic inflammation involving the respiratory tract observed at autopsy." Resp. Ex. C at 5; see also Resp. Ex. J at 3. She stressed that the respiratory tract inflammation involved both the lower and upper respiratory tract. Resp. Ex. J at 4. Given these findings, Dr. Vargas opined N.A. had a respiratory tract viral infection. Id. at 3; Resp. Ex. C at 5; Tr. 172-73. Additionally, N.A.'s twin sister, L.A., had a low-grade fever on July 1, 2016, and a viral cause would be "a likely possibility." Resp. Ex. C at 6 (citing Pet. Ex. 7 at 5 (noting "viral illness" as a differential diagnosis)). She opined that this "could indicate that [L.A.] had whatever viral infection that N.A. had." Tr. 175; see also Resp. Ex. J at 4.

Dr. Vargas explained "[v]iruses with a predilection for the pediatric respiratory tract include rhinoviruses, respiratory syncytial virus, adenoviruses, influenza viruses, parainfluenza viruses, human bocavirus, and human metapneumovirus" and "[i]nfection with respiratory viruses is exceedingly common in children." Resp. Ex. C at 5. Although there were "no reports

of any viral testing conducted as a part of [N.A.'s] autopsy, nor of any bacterial testing,"[72] Dr. Vargas opined "[i]t is expected that had comprehensive testing for viral respiratory pathogens been conducted, it would have likely confirmed viral infection." Id. at 5-6. She added that a virus would explain the chronic inflammation seen in N.A.'s upper and lower respiratory tract and could have caused concomitant chronic inflammation in other organs. Id. at 6. She concluded that such respiratory tract inflammation could not be explained by a vaccination. Id. at 6. During the hearing, Dr. Vargas testified that a viral cause of N.A.'s death remained a "possibility." Tr. 183.

Dr. Vargas also posited that there could have been a bacterial cause of N.A.'s death. Resp. Ex. C at 6; Tr. 186. N.A. had cellulitis in her eye six weeks prior to her death. Resp. Ex. C at 6. Dr. Vargas noted various causes of cellulitis and opined that "these bacteria can spread through the body hematogenously and seed other sites." Id. Additionally, "[o]ccult abscesses and other bacterial infections can be associated with intermittent and persistent fevers, such as was observed in [N.A.]." Id. Dr. Vargas opined it was "possible that the bacterial infection was not fully cured and seated somewhere or had a pocket left and could have been a source of infection . . . rather than the respiratory tract." Tr. 186. Dr. Vargas acknowledged no anatomic sources of infection were identified during autopsy but explained that only a small proportion of N.A.'s tissue was sampled, making it difficult to rule out infection in other unsampled areas. Resp. Ex. C at 6; Tr. 183-84. Here, the cellulitis predated N.A.'s MMRV vaccination, and thus, it would preclude causation. Resp. Ex. C at 6. At the hearing, Dr. Vargas agreed that cellulitis or bacterial infection as a cause of death was only a "possibility." Tr. 182-84, 186.

5. Respondent's Expert, Dr. Christine McCusker, M.D.[73]

a. Background and Qualifications

Dr. McCusker received a B.Sc. in microbiology and immunology, M.Sc. in molecular biology, and M.D. in Ontario, Canada. Resp. Ex. A at 1; Resp. Ex. O at 1. She then completed a pediatric residency, fellowship in immunology, and a fellowship in allergy and immunology. Resp. Ex. O at 2. She obtained board certification from the American Board of Pediatrics and is certified in pediatrics and allergy and clinical immunology in Canada. Id.; Resp. Ex. A at 1. Dr. McCusker's "research focus is the regulation of the immune responses." Resp. Ex. A at 1. She treats an average of 50-120 children per week in allergy and clinical immunology as well as urgent care general pediatrics. Id. at 2. Throughout her career, she has held various university

[72] Dr. Vargas noted "[a] typical autopsy workup in unexpected death includes postmortem microbiologic culture for bacteria." Resp. Ex. C at 6 (citing Resp. Ex. C, Tab 2 (Johan J. Dempers et al., The Institution of a Standardized Investigation Protocol for Sudden Infant Death in the Eastern Metropole, Cape Town, South Africa, 61 J. Forensic Scis. 1508 (2016))). She found it "striking . . . that there [was] no record of any postmortem microbiologic testing." Id.

[73] Dr. McCusker submitted two expert reports and testified at the hearing. Resp. Exs. A, H; Tr. 3. Dr. McCusker's expert reports address theories from Dr. Miller that he abandoned at the hearing, and thus, the undersigned addresses only those opinions from Dr. McCusker that are relevant to this case and Petitioners' theory.

and hospital appointments and she has authored or co-authored over 100 publications. Resp. Ex. O at 3-4, 33-46.

b. Opinion

i. Althen Prong One

Dr. McCusker addressed Petitioners' theory that N.A. suffered her first febrile seizure on the night of her death and this seizure was vaccine-induced. Resp. Ex. A at 9. Dr. McCusker noted Petitioners relied upon Kinney et al. (2009), which found 19 of the 49 SUDC cases had a family or personal history of febrile seizures. Id. (citing Pet. Ex. 18 at 10 tbl.1). She explained that the incidence of febrile seizure or family history of febrile seizures "was not significantly different from controls in this study." Id. (citing Pet. Ex. 18 at 10 tbl.1). Additionally, Kinney et al. studied the frequency of hippocampal and temporal lobe abnormalities; however, only a small number amount of children's hippocampus and temporal lobes were available for examination and some "frequencies were not statistically different." Id. Lastly, Dr. McCusker noted vaccination was not listed as a risk factor in Kinney et al. Id.

Dr. McCusker testified that "there is an increased risk of febrile seizures in family members of those who've had febrile seizures," although the literature is "not particularly strong." Tr. 210. She briefly discussed Hesdorffer et al. and Hefti et al., articles relied upon by Petitioners, and argued that these articles did not find a family history of febrile seizures was significantly increased in SUDC cases, with or without hippocampal abnormalities. Resp. Ex. A at 10 (citing Pet. Exs. 16, 27-28). She determined that an increased risk of febrile seizures in family members "would imply that there are genetic causes of the febrile seizures." Tr. 210.

Next, she explained that there are many similarities in the risk factors for death in SIDS and SUDC cases, including the prone sleeping position and infection or illness, although "an upper respiratory tract infection is considered a risk factor for [SIDS]" and "less so" for SUDC. Tr. 196; see also Resp. Ex. H at 1; Resp. Ex. A, Tab 27 at 3, 3 tbl.1 (noting prone position and mild infections as risk factors for SIDS);[74] Pet. Ex. 18 at 7, 10 tbl.1 (analyzing similarities in SUDC and non-SUDC cases); Pet. Ex. 16 at 7 tbl.2 (listing risk factors for SIDS, SUDC, febrile seizures, and SUDEP); Pet. Ex. 34 at 14 ("Mild infection around the time of death is present in approximately one-half of SIDS infants.").[75] Kinney et al. explained that because these risk factors are not found in all cases, they "are not causative." Resp. Ex. A, Tab 27 at 3. Vaccination was not listed as a risk factor. Resp. Ex. H at 2; see, e.g., Pet. Exs. 16, 18; Resp. Ex. A, Tab 27.

[74] Hannah C. Kinney & Bradley T. Thach et al., Sudden Infant Death Syndrome, 361 New Eng. J. Med. 795 (2009).

[75] Hannah C. Kinney et al., The Serotonergic Anatomy of the Developing Human Medulla Oblongata: Implications for Pediatric Disorders of Homeostasis, 41 J. Chem. Neuroanatomy 182 (2011).

At the hearing, Dr. McCusker explained that theoretically the prone position is a risk factor due to an infant's inability to lift and turn their head, which can lead to an obstructed airway in the bedding or other item in the crib. Tr. 197-98; see also Resp. Ex. A at 13; Resp. Ex. A, Tab 27 at 4, 7. A child (over the age of one) engages in "resistive breathing," where abdominal muscles are used to breathe and the stomach pushes out while breathing. Tr. 198. Thus, when a child is in the prone position, there is more effort engaged to breathe. Id. Dr. McCusker contended that if a child has an upper respiratory infection with an obstructed airway, the prone position can result in a child that is unable to breathe. Tr. 199.

Dr. McCusker cited various articles discussing airway obstruction in SIDS/SUDC and in the presence of upper respiratory infections. Resp. Ex. A at 13-15. She opined that upper respiratory tract infections in infants can cause upper airway obstructions, compromising airway function. Id. at 15; Resp. Ex. H at 2. And unlike vaccination, an upper respiratory tract infections "is a defined risk factor for SIDS, SUDC[,] and SUDEP." Resp. Ex. H at 2.

Bollag[76] explained "[i]nfants and small children have narrow airways," and thus, "[i]nflammation and congestion of the mucosa can result in obstruction very rapidly." Resp. Ex. A, Tab 37 at 1. Children up to the age of two have difficulty when both breathing and feeding through the mouth. Id. Infants breathe through their nose and learn to breathe through their mouth during their first year of life. Resp. Ex. H at 2; see also Resp. Ex. A, Tab 33 at 4;[77] Resp. Ex. A, Tab 38 at 1.[78] Moschino et al. suggested that mucus in upper airways can affect respiratory functions. Resp. Ex. A, Tab 38 at 1. deAlmeida et al.[79] noted "[t]he switch to oral breathing in response to a nasal obstruction is crucial for survival, and has been put forward as an important mechanism in preventing [SIDS]." Resp. Ex. A, Tab 36 at 1; see also, e.g., Resp. Ex. G, Tab 1 at 1 ("It has [] been suggested that blockage of the nasal passages of infants who are obligate nose breathers could result in asphyxia and SIDS. In some infants, nasal obstruction may lead to pharyngeal closure, which may prolong an apnoeic period and exacerbate associated hypoxaemia." (internal citations omitted)).[80]

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[76] Ueli Bollag, Acute Respiration Infections in Childhood: Tackling the Problem at the Level of the Nose, 35 J. Tropical Pediatrics 140 (1989).

[77] W.J. Kleemann et al., Infections of the Upper Respiratory Tract in Cases of Sudden Infant Death, 108 Int'l J. Legal Med. 85 (1995).

[78] L. Moschino et al., Is Nasal Suctioning Warranted Before Measuring 0_2 Saturation in Infants with Bronchiolitis?, 101 Archives Disease Childhood 114 (2016).

[79] Victor L. deAlmeida et al., The Effect of Nasal Occlusion on the Initiation of Oral Breathing in Preterm Infants, 18 Pediatric Pulmonology 374 (1994).

[80] Richard Harding et al., Postnatal Development of Responses to Airflow Obstruction, 22 Clinical & Experimental Pharmacology & Physiology 537 (1995).

Ralston et al.,[81] a clinical practice guideline from the American Academy of Pediatrics, discussed frequent respiratory infections in children and recognized that an upper airway obstruction due to infection can increase the effort of breathing. Resp. Ex. A, Tab 31 at 6. Kleemann et al. compared nasal cavities in SIDS cases to control cases, all under the age of one, and determined rhinitis[82] "seem[ed] to be merely a result of the high incidence of upper respiratory tract infections in this age group." Resp. Ex. A, Tab 33 at 1. The authors "speculate[d] [] that infections of the nose combined with other factors could play a role in [] [SIDS]." Id. at 4. The authors concluded that since infants breathe through their nose and learn to breathe through their mouth during their first year, "even small infections of the nose can cause obstruction of the airway." Id.

ii. Althen Prongs Two and Three

Dr. McCusker found Petitioners' theory "exceedingly unlikely." Tr. 213. Dr. McCusker could not discern how N.A. died. Id. But she found it "highly unlikely that the MMR[V] vaccine played a role in [N.A.'s] death." Id. She explained that even if seizures post-MMRV vaccine occur, "there is no increased frequency of infant death or SUDC in children who receive their MMRV." Tr. 213-14. This "sequence of events" from Petitioners "simply doesn't occur in the children who are at risk for febrile seizures who develop febrile seizures post-MMRV." Tr. 214.

Dr. McCusker classified N.A.'s case as SUDC. Tr. 195. N.A. was described as having her feet sticking through the slacks of the crib upon discovery, which Dr. McCusker believed made it difficult for her to roll over. Tr. 200. She found this prone position increased the possibility of SUDC. Resp. Ex. A at 16; Resp. Ex. H at 3.

Dr. McCusker acknowledged that N.A. was on day seven post-vaccination and was therefore within the risk period of febrile seizures post-MMRV vaccine. Resp. Ex. A at 9, 15; Resp. Ex. H at 3. She noted, however, that even though Petitioners' studies showed febrile seizures occur at an increased frequency seven to 10 days following MMRV vaccination, these studied failed to mention an increased frequency of death (or SUDEP) during this time period. Resp. Ex. A at 9, 15; Resp. Ex. H at 3.

Given the time of death from the medical examiner (between 9:00 p.m. and 10:00 p.m. on the night of June 30, 2016), and N.A.'s receipt of Motrin around 7:00 p.m. the night of June 30, 2016, Dr. McCusker testified that the Motrin "would have been working" at the time of death since it is effective for eight hours. Tr. 211-12. Thus, she opined that N.A. would not have had a fever during this time. Tr. 213. And "any fever she had at that time prior to the [Motrin] would

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[81] Shawn L. Ralston et al., Clinical Practice Guideline: The Diagnosis, Management, and Prevention of Bronchiolitis, 134 Pediatrics e1474 (2014).

[82] Rhinitis is "inflammation of the mucous membrane of the nose." Rhinitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=43725 (last visited Nov. 13, 2023).

have been controlled during the time of her demise, suggesting . . . [a] fever-inducing seizure would be unlikely." Tr. 211.

With regard to the significance of family history of febrile seizures, Dr. McCusker opined that N.A.'s brother with a history of febrile seizures also has a genetic abnormality, a microdeletion in an area associated with neurodevelopmental delays. Tr. 210-11. Based on this, Dr. McCusker opined N.A.'s brother is not at the same "genetic standpoint" as N.A. Tr. 211. She explained that "the familial febrile seizures would not be predicted to be the same risks if the microdeletion is responsible for his . . . susceptibility to febrile seizures." Id.

Dr. McCusker opined N.A. had a viral respiratory infection, which is a risk factor for SIDS and SUDC, for the following reasons. Tr. 200; Resp. Ex. A at 15; Resp. Ex. H at 2-3. First, N.A.'s autopsy revealed small amount of mucous in her nares, trachea, and bronchi and the respiratory mucosa was mildly congested. Tr. 200; Resp. Ex. A at 15 (citing Pet. Ex. 6 at 4). Dr. McCusker also relied upon Dr. Vargas' findings here as it relates to the pathology. Tr. 200. She noted N.A. had a runny nose on the day she died. Id. Although N.A. was noted to be feeling warm on the night of her death, Dr. McCusker found no evidence N.A. had a fever. Resp. Ex. H at 2. She maintained N.A.'s autopsy findings can be "reasonably [] attributed" to an upper respiratory tract infection. Id. And at the hearing, she noted that there are explanations other than vaccination for why a child would develop a fever. Tr. 202-04 (citing Resp. Ex. V).[83]

Additionally, N.A.'s twin sister, L.A., went to the hospital following N.A.'s passing and "was diagnosed with crusting in the nose and what was felt to be a[n] acute viral infection." Tr. 200; see also Resp. Ex. A at 15. N.A.'s brother was diagnosed with an infection 16 days after N.A.'s death, which Dr. McCusker found suggested an acute viral illness was circulating in the family on the night of N.A.'s death. Resp. Ex. A at 15. Given these facts, she concluded that "[i]t [was] possible . . . that [N.A.] may also have had an undiagnosed upper respiratory tract infection leading to airway occlusion in the prone position as suggested by Kinney et al." Id. (citing Pet. Ex. 18); see also Resp. Ex. H at 2.

Dr. McCusker opined that any congestion N.A. had would not have been caused by her MMRV vaccination. Tr. 201. She agreed MMRV vaccination can trigger a fever but "runny nose and crusting of the nose is not a feature of MMRV." Id.

She acknowledged that a finding of an upper respiratory infection would be insufficient to cause asphyxia, but argued that an upper respiratory tract infection can cause upper airway obstruction and, unlike vaccination, an upper respiratory tract infection "is a defined risk factor for SIDS, SUDC[,] and SUDEP." Resp. Ex. H at 2.

Dr. McCusker concluded that N.A. likely had an acute infection at the time of death. Resp. Ex. A at 16; Resp. Ex. H at 2-3. She found no evidence supporting a mechanistic role for MMRV vaccination in N.A.'s death. Resp. Ex. A at 16; Resp. Ex. H at 3.

[83] Caroline Hervé et al., The How's and What's of Vaccine Reactogenicity, 39 NPJ Vaccines 1 (2019).

IV. DISCUSSION

A. Standards for Adjudication

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Hum. Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioners' burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). Petitioners need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006). Instead, Petitioners may satisfy their burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

In particular, Petitioners must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Hum. Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). The received vaccine, however, need not be the predominant cause of the injury. Shyface, 165 F.3d at 1351. A petitioner who satisfies this burden is entitled to compensation unless Respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B). However, if a petitioner fails to establish a prima facie case, the burden does not shift. Bradley v. Sec'y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

"Regardless of whether the burden ever shifts to the [R]espondent, the special master may consider the evidence presented by the [R]espondent in determining whether the [P]etitioner has established a prima facie case." Flores v. Sec'y of Health & Hum. Servs., 115 Fed. Cl. 157, 162-63 (2014); see also Stone v. Sec'y of Health & Hum. Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."); de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the [P]etitioner's evidence on a requisite element of the [P]etitioner's case-in-chief."); Pafford, 451 F.3d at 1358-59 ("[T]he presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination. . . . [T]he Special Master properly introduced the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations.").

B. Factual Issues

Petitioners must prove, by a preponderance of the evidence, the factual circumstances surrounding their claim. § 13(a)(1)(A). To resolve factual issues, the special master must weigh the evidence presented, which may include contemporaneous medical records and testimony. See Burns v. Sec'y of Health & Hum. Servs., 3 F.3d 415, 417 (Fed. Cir. 1993) (explaining that a special master must decide what weight to give evidence including oral testimony and contemporaneous medical records).

Medical records, specifically contemporaneous medical records, are presumed to be accurate and generally "warrant consideration as trustworthy evidence." Cucuras v. Sec'y of Health & Hum. Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). But see Kirby v. Sec'y of Health & Hum. Servs., 997 F.3d 1378, 1382 (Fed. Cir. 2021) (rejecting the presumption that "medical records are accurate and complete as to all the patient's physical conditions"); Shapiro v. Sec'y of Health & Hum. Servs., 101 Fed. Cl. 532, 538 (2011) ("[T]he absence of a reference to a condition or circumstance is much less significant than a reference which negates the existence of the condition or circumstance." (quoting Murphy v. Sec'y of Health & Hum. Servs., 23 Cl. Ct. 726, 733 (1991), aff'd per curiam, 968 F.2d 1226 (Fed. Cir. 1992))), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 503 F. App'x 952 (Fed. Cir. 2013). The weight afforded to contemporaneous records is due to the fact that they "contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium." Id. To overcome the presumptive accuracy of medical records, a petitioner may present testimony which is "consistent, clear, cogent, and compelling." Sanchez v. Sec'y of Health & Hum. Servs., No. 11-685V, 2013 WL 1880825, at *3 (Fed. Cl. Spec. Mstr. Apr. 10, 2013) (citing Blutstein v. Sec'y of Health & Hum. Servs., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)), mot. for rev. denied, 142 Fed. Cl. 247 (2019), vacated on other grounds & remanded, 809 F. App'x 843 (Fed Cir. 2020).

There are situations in which compelling testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. Campbell v. Sec'y of Health & Hum. Servs., 69 Fed. Cl. 775, 779 (2006) ("[L]ike any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking."); Lowrie v. Sec'y of Health & Hum. Servs., No. 03-1585V, 2005 WL 6117475, at *19 (Fed. Cl. Spec. Mstr. Dec. 12, 2005) ("[W]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent." (quoting Murphy, 23 Cl. Ct. at 733). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1379 (Fed. Cir. 2009); Bradley, 991 F.2d at 1575.

Despite the weight afforded medical records, special masters are not bound rigidly by those records in determining onset of a petitioner's symptoms. Valenzuela v. Sec'y of Health & Hum. Servs., No. 90-1002V, 1991 WL 182241, at *3 (Fed. Cl. Spec. Mstr. Aug. 30, 1991); see also Eng v. Sec'y of Health & Hum. Servs., No. 90-1754V, 1994 WL 67704, at *3 (Fed. Cl.

Spec. Mstr. Feb. 18, 1994) (Section 13(b)(2) "must be construed so as to give effect also to § 13(b)(1) which directs the special master or court to consider the medical records (reports, diagnosis, conclusions, medical judgment, test reports, etc.), but does not require the special master or court to be bound by them").

C. Causation

To receive compensation through the Program, Petitioners must prove either (1) that N.A. suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that she received, or (2) that N.A. suffered an injury that was actually caused by a vaccination. See §§ 11(c)(1), 13(a)(1)(A); Capizzano, 440 F.3d at 1319-20. Petitioners must show that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface, 165 F.3d at 1352-53).

Because Petitioners do not allege N.A. suffered a Table Injury, they must prove a vaccine N.A. received caused her injury. To do so, Petitioners must establish, by preponderant evidence: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen, 418 F.3d at 1278.

The causation theory must relate to the injury alleged. Petitioners must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen v. Sec'y of Health & Hum. Servs., 35 F.3d. 543, 548-49 (Fed. Cir. 1994). Petitioners cannot establish entitlement to compensation based solely on their assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether a petitioner is entitled to compensation, the special master shall consider all material in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in Petitioners' favor when the evidence weighs in their favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in a petitioner's favor).

Testimony that merely expresses the possibility—not the probability—is insufficient, by itself, to substantiate a claim that such an injury occurred. See Waterman v. Sec'y of Health & Hum. Servs., 123 Fed. Cl. 564, 573-74 (2015) (denying a petitioner's motion for review and noting that a possible causal link was not sufficient to meet the preponderance standard). The Federal Circuit has made clear that the mere possibility of a link between a vaccination and a petitioner's injury is not sufficient to satisfy the preponderance standard. Moberly, 592 F.3d at 1322 (emphasizing that "proof of a 'plausible' or 'possible' causal link between the vaccine and the injury" does not equate to proof of causation by a preponderance of the evidence); Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019). While certainty is

by no means required, a possible mechanism does not rise to the level of preponderance. Moberly, 592 F.3d at 1322; see also de Bazan, 539 F.3d at 1351.

V. FACTUAL ANALYSIS

As Federal Circuit precedent establishes, in certain cases it is appropriate to determine the nature of an injury before engaging in the Althen analysis. Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1346 (Fed. Cir. 2010). Since "each prong of the Althen test is decided relative to the injury[,]" determining facts relating to the claimed injury can be significant. Id. Here, the parties have identified two factual issues. First, they dispute whether N.A. suffered a seizure during the night of June 30, 2016 or the morning of July 1, 2016. Joint Prehearing Submission at 4. Next, they dispute whether N.A.'s autopsy slides show abnormalities in the hippocampus, specifically granule cell dispersion and/or bilamination of the dentate gyrus. Id. Additionally, Dr. Miller opines that N.A. had abnormalities in the medulla. See Pet. Ex. 22 at 5, 8; Pet. Ex. 65 at 3; Tr. 23, 46-49.

A. There Is Not Preponderant Evidence That N.A. Suffered a Seizure

The undersigned finds that Petitioners did not prove by preponderant evidence that N.A. suffered a seizure prior to her death.

The first reason for this finding is based on N.A.'s individual history. She did not have a history of seizures, febrile, or otherwise. None of her medical records identify a history of any prior seizures. During periods of prior illness, when N.A. had a fever, she did not experience a seizure. Her parents were both health care providers, and they provided detailed histories during N.A.'s medical appointments and during the investigation of N.A.'s demise. N.A. had previous illnesses, including upper respiratory infections and cellulitis, but during these illnesses, she did not experience a febrile seizure. She had also received routine childhood vaccinations prior to the vaccination at issue, and she did not have a febrile seizure associated with her vaccinations. On the evening prior to her demise, N.A.'s mother noted that she had a low-grade fever and Motrin was administered. Her low-grade fever was not elevated to the level that is reportedly associated with febrile seizures. See, e.g., Pet. Ex. 16 at 3 ("[Febrile seizures] were defined as a seizure associated with illness or fever of ≥ 101°F . . . ."); Resp. Ex. E, Tab 4 at 2 ("The most significant risk factor for the development of a first febrile seizure is the height of the temperature; the higher the temperature, the higher the likelihood of a febrile seizure. . . . Most children have a temperature of at least 39°C at the time of a seizure.").[84]

In summary, there is no evidence from N.A.'s history to suggest that she ever had a seizure, or that illnesses or vaccinations which cause fever ever triggered a seizure.

N.A. did have a family history of febrile seizures; her brother had several febrile seizures. The medical literature shows that this fact may have increased N.A.'s risk to have a febrile seizure, but this increased risk does not equate to preponderant evidence. See Tr. 58, 60, 62 (Dr. Miller testifying that this is a "rare event").

[84] 39°C is 102.2°F.

Next, Dr. Virani, the pathologist who conducted the autopsy, did not opine or suggest that a seizure was a contributing factor to the cause of death. Moreover, N.A.'s case was reviewed by the SUDCRRC, and they conducted a thorough investigation, including a review of records, histology tissue review by a cardiac pathologist and neuropathologist, and genetic analyses. They did not conclude that N.A. had a seizure.

Further, there was no physical evidence to suggest that N.A. had a seizure. As explained by Crandell et al., "[p]ostmortem evidence of [a] terminal seizure is often absent or nonspecific." Pet. Ex. 72 at 7. "Common stigma" may include tongue biting or urinary incontinence. Id. Due to N.A.'s age, urinary incontinence could not be evaluated. But there is no sign or description in the autopsy to suggest tongue biting. Thus, there is no physical evidence to support the conclusion that that N.A. had a seizure.

Dr. Virani noted pulmonary edema in his autopsy, but he did not opine that the finding suggested or supported febrile seizure as a cause of death. Dr. Kinbsourne mentioned pulmonary edema as a finding in support of a seizure, but he did not provide supportive evidence for his opinion. Devinsky did not explain why pulmonary edema would occur due to a seizure as opposed to another cause of death. And Kloster and Engelskjøn described pulmonary edema as a non-specific finding. Moreover, Dr. Miller did not opine that the presence of pulmonary edema was significant to him. And none of the pathologists offered opinions about the finding of pulmonary edema. The only pathologist with special expertise in pulmonary pathology is Dr. Vargas,[85] and she did not see evidence of pulmonary edema in the lung tissue. Resp. Ex. C at 4. The undersigned finds that the finding of pulmonary edema on autopsy does not support a conclusion that a febrile seizure occurred or caused N.A.'s death.

Dr. Kinsbourne testified that the body configuration suggested a seizure, but he did not explain what about the configuration weighed in favor of finding that a seizure occurred. Further, he did not cite any foundational evidence in support of this opinion. Dr. Vargas rejected Dr. Kinsbourne's opinion that there was any unusual posture that suggested a seizure. Her opinion on this topic is more persuasive, especially given that Dr. Vargas is a practicing pathologist, and Dr. Kinsbourne is long removed from clinical practice and does not have expertise in forensic pathology or death investigations.[86]

In conclusion, there is not preponderant evidence that N.A. had a febrile seizure that caused or contributed to her death.

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[85] See Resp. Ex. Q at 1-3 (noting a residency in anatomic and clinical pathology, fellowship in pediatric pathology, hospital appointments as a pathologist, and Director of Pulmonary Pathology at Boston Children's Hospital); Tr. 161 (noting a pulmonary pathology fellowship and a fellowship in pediatric pathology).

[86] See Pet. Ex. 14 (noting no expertise in forensic pathology); Tr. 90 (noting he is no longer a practicing physician since 1981).

B. There Is Not Preponderant Evidence of Hippocampal or Medullary Abnormality

At least five neuropathologists and/or forensic pathologists reviewed the brain tissue and only Dr. Miller observed any abnormality.

The pathologist of record, Dr. Virani, took sections of the brain for microscopic analysis and did not observe any abnormalities. See Nordwall ex rel. Tori v. Sec'y of Health & Hum. Servs., 83 Fed. Cl. 477, 488 (Fed. Cl. 2008) ("An autopsy report by a medical examiner is without question a contemporaneous medical record" that "warrant[s] consideration as trustworthy evidence."). As part of the SUDCRRC case review, the brain tissue was reviewed by a neuropathologist. The report states that the neuropathologist reviewed three brain slides and found "no significant histopathology." Pet. Ex. 77 at 8. In addition, forensic pathologist reviewers reviewed all 12 autopsy slides. The SUDCRRC study review "was in general agreement with the pathologist of record." Id. Thus, the SUDCRRC pathologists agreed with Dr. Virani's assessment that there were no abnormalities of the brain tissue.

Dr. Miller observed abnormalities of the hippocampus, specifically dysplasia of the dentate gyrus and granule cell dispersion and bilamination, and abnormal areas of the medulla, lacking in neurons. In response to photomicrographs showing these "abnormalities," Dr. Lidov opined that Dr. Miller magnified images and failed to show the entire field, which had the effect of making some tissue appear to show abnormalities. Regardless, Dr. Lidov did not observe any abnormalities of the hippocampal or medullary tissue.

Lastly, Dr. Vargas reviewed the brain tissue and opined there was no pathology.

Therefore, the undersigned finds that there is not preponderant evidence that N.A. had hippocampal or medullary abnormalities or any other brain abnormality.

VI. CAUSATION ANALYSIS

A. Althen Prong One

Under Althen prong one, Petitioners must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu, 569 F.3d at 1375; Pafford, 451 F.3d at 1355-56. Petitioners' theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable" medical or scientific explanation. Boatmon, 941 F.3d at 1359; see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If Petitioners rely upon a medical opinion to support their theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen, 618 F.3d at 1347 ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994)

(stating that an "expert opinion is no better than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

The undersigned acknowledges that the parties have stipulated that the MMRV vaccine can cause febrile seizures. For the following reasons, however, the undersigned finds Petitioners have failed to provide preponderant evidence of a sound and reliable theory to explain how the MMRV vaccine can cause a seizure in a vulnerable child which can lead to death.

Petitioners' experts have opined that the MMRV vaccine caused a febrile seizure in the context of hippocampal and medullary brain abnormalities, rendering the child vulnerable to sudden unexplained death. As such, Petitioners' theory of causation relies on two factual presumptions: (1) that a febrile seizure occurred before death and (2) that there were brain abnormalities that increased the risk of sudden death. Because there is not preponderant evidence of these facts, Petitioners' causal theory fails. Even if there was factual support for Petitioners' theory, there are additional reasons why the undersigned finds that Petitioners have failed to provide evidence of a sound and reliable theory by preponderant evidence.[87]

First, the language used by both Dr. Miller and Dr. Kinsbourne to express their opinions suggests they hold their opinions to a lower threshold than the preponderant standard required by the Vaccine Act. Dr. Miller uses the phrase "medically plausible." See Pet. Ex. 22 at 9 ("[T]here is a scientifically and medically plausible means to connect these events."); Pet. Ex. 22 at 13 ("This chain of events represents a highly plausible, scientifically valid, hypothesis."). "Medical plausibility," however, is insufficient to reach the standard required. See, e.g., Boatmon, 941 F.3d at 1359-60 (citing Federal Circuit case law "reiterat[ing] that a 'plausible' or 'possible' causal theory does not satisfy the standard"); Moberly, 592 F.3d at 1322 (finding Petitioners' characterization that the vaccine "likely caused" the injury to appear "closer to proof of a 'plausible' or 'possible' causal link between the vaccine and the injury, which is not the statutory standard"); LaLonde v. Sec'y of Health & Hum. Servs., 746 F.3d 1334, 1339 (Fed. Cir. 2014) ("[W]e have made clear that simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof.").

In Boatmon, the Federal Circuit found that Dr. Miller[88] presented a theory that was "only 'plausible.'" Boatmon, 941 F.3d at 1360. The Circuit found that the characterization of the standard of proof as "plausible" was "incorrect as a matter of law." Id. Application of the holding in Boatmon renders Dr. Miller's opinions insufficient here. Thus, the undersigned finds that Dr. Miller did not prove by preponderant evidence a sound and reliable causal theory to satisfy Althen prong one.

[87] In other words, the undersigned's rulings as to the factual predicates proposed by Petitioners are not determinative as to Althen prong one. There are independent reasons that the undersigned finds Petitioners have failed to prove Althen prong one as explained herein.

[88] Dr. Miller is the same expert who testified on behalf of the Petitioners in Boatmon. See Boatmon, 941 F.3d 1351.

Dr. Kinsbourne also used words that reflect a lower burden of proof. For example, he testified that unobserved seizures "undoubtedly" occur and can cause death. Tr. 84-85; see also Pet. Ex. 61 at 3 ("The rarity of death . . . does not suggest that unwitnessed febrile seizures don't cause death."). Both experts couched their opinions in terms of "significant," "elevated," or "increased risk." They stated there was an "increased risk" of febrile seizure. Pet. Ex. 22 at 8; Pet. Ex. 61 at 2. They also cited medical literature that used the same phrase or similar phrases. See, e.g., Pet. Ex. 16 at 1 ("[T]erminal fever may increase the risk for an unwitnessed terminal seizure"); Pet. Ex. 72 at 7 ("We speculate that [febrile seizures] occur in some children without a known [febrile seizures] history . . . ."). An increased risk, however, is not the same as preponderant evidence of seizures. See, e.g., Pet. Ex. 21 at 6 (explaining "potential benefits must be balanced by the increased risk (albeit small) of febrile seizures"); Resp. Ex. E, Tab 1 at 2 (discussing "the rarity of death during febrile convulsions"); Resp. Ex. U at 3 ("The mortality associated with febrile seizures is extremely low."); Resp. Ex. L at 2 (noting "the absolute risk of death [from febrile seizure] [is] [] very low"). As the medical literature aptly establishes, an increased risk of having a seizure, when the likelihood is still very low, does not rise to the level of preponderant evidence.

Next, the part of Petitioners' causal theory based on pathological abnormalities is controversial, particularly the hypothesis advanced by Dr. Kinney and her colleagues related to hippocampal abnormalities. Literature filed by Respondent's experts suggest that the hippocampal abnormalities described by Kinney et al. are not pathological but may be "normal variants" and not unique to children who have seizures or epilepsy. See, e.g., Resp. Ex. I, Tab 1 at 18. In 2020, Roy et al. studied pediatric hippocampal tissue from 147 autopsies and found that "granule cell dispersion is within the spectrum of normal variation." Id. at 1. Another smaller study, also published in 2020, from a group at Yale reported "[their] failure to identify a significant relationship between the frequency or type of hippocampal lesions among patients with and without a history of seizure, or with lifetime seizure frequency, suggests that pathophysiological conclusions should remain tentative." Resp. Ex. J, Tab 5 at 8. And in 2021, Leitner et al. conducted a blind review of hippocampal tissues in sudden death cases, and reported a "lack of an association of hippocampal findings in SUDC and controls, as well as inconsistency of observations by multiple blinded reviewers, indicat[ing] discrepancy with previous studies." Resp. Ex. K at 2.

In short, current studies question the significance of hippocampal abnormalities and the relationship between such abnormalities and seizures and/or sudden death. There is no consensus on these issues and more research is recommended. Thus, the undersigned finds that Petitioners' reliance on hippocampal abnormalities as part of their theory is not sound or reliable. The undersigned also finds that Petitioners' reliance on the idea that hippocampal abnormalities cause children to be vulnerable and at risk of sudden death is likewise not sound or reliable.[89]

Further, the Petitioners' theory is not sound and reliable because they have extrapolated information taken from studies that relate to children with epilepsy (SUDEP) and applied it to

[89] Whether N.A. had or did not have hippocampal abnormalities is not determinative of the undersigned's finding as to Althen prong one. There are other independent reasons for the undersigned's determination as described herein.

children who do not have epilepsy or a history of prior seizures. The studies cited note comparisons between SUDC and SUDEP, and question whether the pathophysiology which leads to fatal seizures in children with epilepsy may be relevant to unexplained deaths of children, but they do not reach any conclusions that are transferable to the facts and circumstances here.

Dr. Miller testified that the mechanism in SUDC is "similar or identical" to the hypothesis described in SUDEP. Tr. 68. Several articles cited by the experts discuss this subject. For example, Kon et al. noted that hippocampal abnormalities are associated with epilepsy and are thought to predispose individuals to seizures. But this hypothesis is not well studied and more research is needed, as explained in the case report by Dlouhy et al.

Moreover, there is not preponderant evidence that febrile seizures alone in a child without epilepsy can lead to seizure-induced death. Dlouhy et al. noted that febrile seizures are thought to be benign, and they stated that "no reported cases of febrile seizure-induced death have been documented." Pet. Ex. 70 at 2. The authors propose that the same pathophysiological mechanism that occurs in SUDEP could explain some cases of SUDC. Id. at 4. The process thought to occur in SUDEP starts with a generalized tonic-clonic seizure, which leads to "respiratory dysfunction and hypoxemia," and it is "exacerbated by [the child] being facedown in bed, during sleep, and which ultimately leads to bradycardia and asystole." Id. at 3. The disconnect is that children with epilepsy may have genetic mutations or brain abnormalities distinct from other children. Dlouhy et al. describes some of these mutations (Dravet syndrome, temporal lobe epilepsy, and other genetic abnormalities that encode ion channels). Id. at 4. However, it is premature to conclude that the mechanism at play in children with epilepsy could explain deaths in children without epilepsy. As the authors in Dlouhy et al. state, "[f]urther study is needed." Id. They also state that "further evidence may support that . . . some cases of sudden death are induced by provoked seizures," but they do not conclude that the current evidence supports such a finding. Id.; see also Resp. Ex. L at 1-2 (finding "the hypothesis that febrile seizures are associated with an increased risk of death" to not be supported by large study in Denmark where the "increased risk of death after febrile seizure was seen only in children with complex febrile seizures and in those with underlying neurological abnormalities"); Pet. Ex. 74 at 3 tbl.1, 8-9 (showing genetic associations in febrile seizures, SUDC, and SUDEP).

In summary, Petitioners have failed to offer preponderant evidence of a sound and reliable medical theory in support of their claim. Thus, the undersigned finds Petitioners have failed to provide preponderant evidence with respect to the first Althen prong.

B. Althen Prong Two

Under Althen prong two, Petitioners must prove by a preponderance of the evidence that there is a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." Capizzano, 440 F.3d at 1324 (quoting Althen, 418 F.3d at 1278). "Petitioner[s] must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury.'" Pafford, 451 F.3d at 1356 (internal citations omitted).

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen, 418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. Petitioners need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, Petitioners may satisfy their burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

Since Petitioners failed to prove the factual predicates underlying their theory, and failed to prove Althen prong one, it follows that they cannot prove Althen prong two. To summarize, Petitioners' experts opined that the MMRV vaccination administered to N.A. on June 23, lead to a fever on June 30, that provoked a seizure that night, which caused N.A.'s death. Since the undersigned finds that Petitioners' have failed to establish preponderant evidence that N.A. had a seizure, there is no logical sequence of cause and effect. Similarly, Petitioners' experts opined that N.A. had an underlying vulnerability due to her brain abnormalities. As the undersigned finds that Petitioners did not prove N.A. had brain abnormalities by preponderant evidence, the undersigned also finds that she did not have a vulnerability which put her at risk for a seizure. As Petitioners have not proven this aspect of their theory by preponderant evidence, the undersigned finds that they have failed to show by preponderant evidence a logical sequence of cause and effect.

Further, none of N.A.'s treating physicians or pathologists who conducted the autopsy or the SUDCRRC case review attributed N.A.'s death to either a seizure or her vaccinations. Dr. Virani opined that the cause of death was asphyxia. There is no suggestion in his report that he causally associated her death to a seizure or her MMRV vaccination. Several pathologists participated in the SUDCRRC case review, including a cardiologist, neuropathologist, and forensic pathologist. They concluded that N.A.'s cause of death was "[u]nexplained sudden death" and the manner of death was "[u]ndetermined." Pet. Ex. 77 at 9. While they noted the fact that N.A. had received her MMRV vaccination, they did not attribute her death to a seizure or to her vaccination. See Capizzano, 440 F.3d at 1326 (noting "treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen, 418 F.3d at 1280)); Cucuras, 993 F.2d at 1528 (explaining medical records are generally more reliable because they are created contemporaneously with the treatment of the vaccinee).

Regarding the brain abnormalities, Dr. Miller conceded that dentate gyrus dysplasia is a very common finding in all ages and all types of deaths. This observation suggests that dysplasia is a non-specific finding, not unique to SUDC, and not supportive of Petitioners' theory that N.A. had a vulnerability due to her abnormal brain tissue.

Next, the undersigned finds that Petitioners' experts offered opinions about underlying presumptions based on statistics. For example, Dr. Miller's opinion that N.A.'s fever was based on her vaccination and not on her viral infection was based on statistics. He was asked to discuss the cause of N.A.'s fever in light of the fact that her sister was diagnosed with a viral infection the day after N.A.'s death. Specifically, Dr. Miller was asked how he could be certain N.A.'s fever was from the vaccine instead of a potential virus. Dr. Miller responded that he based his answer on

> [s]tatistics. . . . [C]hildren get colds, and they don't generally die of them. They don't generally have fever with colds. There is a described increased risk for both fever and febrile seizures in children who got the MMRV vaccine compared to children who got all other vaccines, including the MMR without the V. It's a significantly increased risk. It's still a very rare event, but it's a definite increased incidence.

Tr. 60.

Similarly, Dr. Kinsbourne testified that a child is "seven times more likely" to have a seizure after MMRV vaccination. Tr. 79. He was unable, however, to reference the citation for this statistic. Regardless, he was using statistical data to support his opinion that N.A. had a seizure after vaccination.

It would be error for the undersigned to accept Dr. Miller's and Dr. Kinsbourne's opinions about what happened to N.A. based on statistics. In Boatmon, the Circuit found "the Special Master's determination that [the child] had a brainstem abnormality rested in part on an assumption based on statistics." Boatmon, 941 F.3d at 1362-63. And this is insufficient proof of causation. See id. at 1363 (explaining the Circuit has "previously rejected statistical likelihood alone as proof of actual causation"); see also Knudsen, 35 F.3d at 550 (rejecting a theory based on a "bare statistical fact").

For these reasons, as well as the reasons described above as they relate to the factual findings specific to N.A., the undersigned finds Petitioners have failed to show by preponderant evidence that there is a logical sequence of cause and effect showing N.A.'s MMRV vaccine caused a fatal seizure or otherwise caused her death.

Accordingly, the undersigned finds that Petitioners have failed to provide preponderant evidence of a logical sequence of cause and effect to satisfy their burden under Althen prong two.

C. Althen Prong Three

Althen prong three requires Petitioners to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That term has been defined as a "medically acceptable temporal relationship." Id. Petitioners must offer "preponderant proof that the onset of symptoms occurred within a time frame for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer

causation-in-fact." de Bazan, 539 F.3d at 1352. The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen prong one). Id.; Koehn v. Sec'y of Health & Hum. Servs., 773 F.3d 1239, 1243 (Fed. Cir. 2014); Shapiro, 101 Fed. Cl. at 542; see also Pafford, 451 F.3d at 1358. A temporal relationship between a vaccine and an injury, standing alone, does not constitute preponderant evidence of vaccine causation. See, e.g., Veryzer, 100 Fed. Cl. at 356 (explaining that "a temporal relationship alone will not demonstrate the requisite causal link and that [P]etitioner must posit a medical theory causally connecting the vaccine and injury").

The parties stipulate that there is a temporal association here. Joint Prehearing Submission at 4 ("Most [MMRV] vaccine related seizures occur [seven] to 10 days after a child has received the MMRV vaccine."). Dr. Miller and Dr. Kinsbourne both opined that the MMRV vaccine can lead to fevers and seizure seven to 10 days after vaccination. Respondent's experts did not disagree. Therefore, the undersigned finds that Petitioners have provided preponderant evidence satisfying Althen prong three. However, a temporal association, without more, is insufficient. Moberly, 592 F.3d at 1323; Grant, 956 F.2d at 1148 ("[A] proximate temporal association alone does not suffice to show a causal link between the vaccination and the injury."). Therefore, Petitioners are not entitled to compensation.

VII. CONCLUSION

This is a heartbreaking case. The undersigned extends her sympathy to Petitioners for their terrible loss. The undersigned's Decision, however, cannot be decided based upon sympathy, but rather on the evidence and law.

For the reasons discussed above, the undersigned finds that Petitioners have failed to establish by preponderant evidence that N.A.'s MMRV vaccination caused her death. Therefore, Petitioners are not entitled to compensation and the petition must be dismissed.

In the absence of a timely filed motion for review pursuant to Vaccine Rule 23, the Clerk of Court **SHALL ENTER JUDGMENT** in accordance with this Decision.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master